

# ABSTRACTS OF WORLD MEDICINE

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## Hygiene and Public Health

### 432. Ecological Observations on Forest Mosquitoes of an Endemic Yellow Fever Area in Panama

P. GALINDO, S. J. CARPENTER, and H. TRAPIDO. *American Journal of Tropical Medicine [Amer. J. trop. Med.]* 31, 98-137, Jan., 1951. 5 figs., 17 refs.

The investigation reported in this paper followed the recognition in January, 1949, of several human cases of sylvan yellow fever in an area east of Panama City. Sites were selected for 11 stations in Central Panama and in the Canal Zone. Larvae of forest mosquitoes were collected weekly in bamboo traps, natural breeding places such as tree holes, and miscellaneous water containers. Detailed observations were made of distribution, breeding habits, mating, egg-laying, and biting activities of diurnal forest mosquitoes; these are reported fully. The larvae of *Sabettus cyaneus* and *Sabettus chloropterus* occur in a specialized type of tree hole which holds water throughout the dry season, and appear to be the only diurnal mosquitoes in the area capable of carrying on in the three months of the dry season when the adults of *Haemagogus* and *Aedes* spp. virtually disappear. The authors suggest that the host relationship of these species with the primates inhabiting the forest and their potential ability to transmit the virus of yellow fever should be carefully studied.

[The observations reported in this paper cannot be adequately abstracted and those interested are advised to study the original paper.]

J. L. Markson

### 433. Scientific Studies on the Cleansing of Drinking Glasses

L. R. BISHOP, T. J. WARD, and C. A. KLOSS. *Journal of the Institute of Brewing [J. Inst. Brew.]* 57, 106-117, March-April, 1951. 3 figs., bibliography in the text.

Although for a number of reasons pathogenic organisms do not multiply in beer, and although the glass containers in which beer is served are more hygienic than the chinaware used for other drinks, much attention has recently been given to the problem of improving the state of the glasses in which beer is served. Of the various ways by which these glasses might be sterilized, the use of washing machinery is open to the objections of difficulty of use during the rush hours, the space it occupies, and the cost of installation and maintenance. Sterilization by hot water is not satisfactory because it is difficult to maintain the water at the required temperature, at which in any case it is too hot for the hands of the workers, in addition to cracking the glasses.

The authors discuss the possibility of solving the problem by the addition of some sterilizing agent to the rinse water. The many preparations which have been tried out have suffered from one or more of a number of objections: their toxicity to human beings, their irritation of the skin or mucous membrane, their corroding effect on metal sinks, their effect on rubber, their unpleasant smell or unpleasant flavour, the production of a haze in beer, and the slow development of their toxic effect on bacteria. Some of the quaternary ammonium compounds have been found to combine rapid toxicity to bacteria with an absence of serious objections on most of these counts; they also possess a fairly well marked detergent action. The rapid lethal action of these compounds is probably the result of their surface activity, which causes a breakdown of the cell protoplasm and leakage of the cell contents.

This report outlines the preliminary experiments carried out on quaternary ammonium compounds under conditions as close as possible to the heaviest contamination likely to occur in practice, the survival of indicator organisms being studied by culture on MacConkey agar. In certain concentrations all the compounds tested were effective within quite short times. Their detergent action was quite satisfactory—though they would not remove lipstick without rubbing.

One marked disadvantage of these preparations is their effect on the retention of the head of the beer, even in small doses. Having regard to the many special effects of the different bactericides, "fixanol C" was considered to be the preparation of choice. This was found to be very effective in maintaining the sterility of the water in the wash-bowl. When the glasses were later dried with a cloth which had been washed the previous night in a solution of this compound and then dried, very few organisms could be recovered from the glasses or from the cloth. This preparation, however, cannot be made in the necessary quantities, so for later tests "fixanol VR", though less effective, was used.

Other disadvantages of using these compounds are the slipperiness of the glasses (though the increase in breakages was only temporary) and foaming in the wash-bowl. These two effects, however, can be got over by the use of a double sink, the quaternary compound being added to the first. The cost of treating the glass-washing water with quaternary compounds is not high and a simple appliance for ensuring the automatic addition of the correct amount of the compound is described.

Carol Thomas

**434. A Study of Reactions following Administration of Crude and Purified Diphtheria Toxoid in an Adult Population**

A. M. PAPPENHEIMER, G. EDSALL, H. S. LAWRENCE, and H. J. BANTON. *American Journal of Hygiene [Amer. J. Hyg.]* 52, 353-370, Nov., 1950. 1 fig., 22 refs.

In view of recent work which has shown that there has been an increase in cases of adult diphtheria since the war and that the proportion of Schick-negative adults may be as low as 15%, a study was made of the Schick status of approximately 3,000 U.S. Army personnel. At the same time observations were made on the local and systemic reactions produced by toxoids of varying degrees of purity. The men were divided into 7 groups of 400, each group receiving a different batch of toxoid and all receiving the Schick test (0.08 units of crude toxoid) and Schick control. All toxoids were diluted to contain 10 flocculating units per ml.; the Schick-test material contained 1/50 MLD in 0.1 ml. Crude toxoid, toxoid partially purified by ammonium sulphate fractionation, and toxoid highly purified by alcohol fractionation were used, the purity of the 3 types of preparation being 20%, 70%, and 95% respectively on the basis of protein-nitrogen content.

The first examinations were carried out 18 to 20 hours after inoculation. Men showing local or systemic reactions (approximately 10 to 20% of all men in any given group) were again examined 24 hours later. Of all men 40% were Schick-positive, the highest proportion (50%) being in the under-20 age group and the lowest (36%) in the over-35 age group. The frequency of allergic reactions to toxoid increased in the older age groups. With crude toxoid, the incidence of local reactions remained almost constant in all age groups, but partially purified toxoid gave significantly fewer reactions in the younger groups as compared with the older groups. The same gradation was seen with the purest toxoid and in the frequency of systemic reactions.

As would be expected, there were few local or systemic reactions in Schick-positive subjects. Injection of highly purified toxoid produced significantly fewer and less severe reactions than those obtained with an equivalent dose of crude toxoid in Schick-negative subjects. Almost all individuals showing local or systemic reactions gave an allergic response to the Schick control inoculation, irrespective of the result of the Schick test itself; men showing a "two plus" reaction to the control test almost invariably had a marked systemic reaction to crude toxoid, and approximately 50% reacted similarly to purified toxoid.

In confirmation of the results of others it was found that there is an inverse correlation between the titre of serum antibody and the flocculation time of the toxoid.

J. F. McCrea

**435. Medical Significance of the Census**

W. P. D. LOGAN. *British Medical Journal [Brit. med. J.]* 1, 720-722, April 7, 1951. 1 fig., 12 refs.

The census is necessary for the calculation of those indices used in measuring the state of the public health. Knowledge of the sex and age distribution of the popu-

lation is essential for correcting the crude indices and revealing the true changes with time. In addition, the construction of national life tables and calculation of the expectation of life can be carried out accurately only from the census figures. Occupational mortality can be deduced by analysing the occupations of the living, as returned in the census, and the occupations of those dying in 1950-52, as given at registration of death. By analysing deaths of married women according to the occupation of their husbands it is hoped to distinguish between socio-economic and occupational factors. Calculation of infant mortality according to the occupation and social class of the father will also be made. There will be no attempt to enumerate the sick, as previous experience has shown the unreliability of the results.

M. Lubran

**436. Death Toll from Rheumatic Fever in Childhood**

G. WOLFF. *Journal of the American Medical Association [J. Amer. med. Ass.]* 145, 719-724, March 10, 1951. 1 fig., 13 refs.

The mortality from rheumatic fever and its consequences in children aged 5 to 19 years in the U.S.A. was assessed by adding the deaths from all forms of heart disease to the deaths from acute rheumatic fever. By combining the average number of deaths for 1939-41 with the census figures for 1940, analysis according to age, sex, race, and geographical division has been made. The mean death rate in this period was 11.7 per 100,000, the mortality increasing with age. In general, girls showed a higher mortality than boys, except in the 15-to-19 age group in white children. The mortality among white children was lower than among non-white children at all ages. Geographically, the mortality was lowest in the southern and highest in the northeastern divisions.

Mortality rates for the whole population were determined up to 1948. They showed a steady decrease to about two-thirds of the 1939-41 level. The sex, race, and geographical distribution of deaths from rheumatic disease of the heart show many similarities with deaths from tuberculosis and suggest that, as in that disease, social and economic factors are important.

M. Lubran

**437. Statistical Studies of Heart Disease. IX. Race and Sex Differences in the Trend of Mortality from the Major Cardiovascular-Renal Diseases**

I. M. MORIYAMA and T. D. WOOLSEY. *Public Health Reports [Publ. Hlth Rep., Wash.]* 66, 355-368, March 23, 1951. 4 figs., 9 refs.

Mortality in the U.S. from "major cardiovascular-renal diseases", comprising all forms of nephritis, infections of the heart (excluding syphilis and acute rheumatic fever), functional heart disease, chronic myocarditis, coronary artery disease, and intracranial lesions of vascular origin, has been analysed according to age, sex, and race; the yearly changes in the period 1920 to 1948 have been determined. Among white females the death rate has fallen over this period, but to a lesser degree in each successive 10-year age group up to 84 years.

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Above this age it has increased, probably owing to "senility" being replaced as a cause of death on death certificates by "cardiovascular disease". For non-whites the death rate is steady or decreasing in all age groups, the trends being similar for males and females. Among white males there was marked increase in death rate in the age groups 35 to 64 years during this period, the other age groups showing a fall or remaining steady.

In the youngest age group (25 to 34) the death rate for non-whites is much greater than for whites. The difference becomes progressively less in the higher age groups, and in the age group 65 to 74 the rates are equal. Above this age the death rate for whites is greater than for non-whites. This reversal is probably not significant, as a similar change is found when deaths from all causes are considered. It may be due to under-registration of deaths and age inaccuracies in death certificates for negroes.

In 1920 the male and female death rates were about the same at all ages, but in 1947 the male rate was about double the female at all ages. The increase in the death rate for white males is statistically significant and does not occur when death rates from all causes are considered. The difference in trends for males and females is most marked in diseases of the heart and chronic nephritis.

M. Lubran

**438. Q Fever Studies in Southern California. Summary of Current Results and a Discussion of Possible Control Measures**

R. J. HUEBNER and J. A. BELL. *Journal of the American Medical Association* [J. Amer. med. Ass.] 145, 301-305, Feb. 3, 1951. 4 figs., 24 refs.

This is a summary of the work done on Q fever in the Los Angeles area since 1947, when it was first recognized there. Its discovery was followed by studies on cattle and milk, a survey of 300 clinical cases, and epidemiological studies embracing almost 10,000 persons. Antibodies against Q fever were demonstrated in 30 widely separated herds and in the pooled milk of many dairies: 45% of those affected resided within a quarter-mile (0.4 km.) of a dairy, the occupation of 38% brought them into contact with livestock, and 32% had used raw milk in their households.

Agglutination tests in various occupational groups gave 23% positive results in the dairy trade, 21.6% in fat-rendering plants, and 16% in hide and wool plants, compared with 1.4% in the aircraft industry. Pasteurization of all milk supplies and vaccination of exposed persons are immediately practicable measures, but effective defence depends on the control of animal reservoirs of infection.

W. G. Harding

**439. Observations on the Epidemiology of Q Fever in Northern California**

E. H. LENNETTE and W. H. CLARK. *Journal of the American Medical Association* [J. Amer. med. Ass.] 145, 306-309, Feb. 3, 1951. 12 refs.

Outbreaks of Q fever in California have been associated with a high percentage of positive agglutination reactions in sheep, goats, and cattle herds respectively. It is

suggested that animal excreta and secretions infected with rickettsiae may be potent sources of infection, possibly by dust spread followed by ingestion or inhalation.

W. G. Harding

**440. Poliomyelitis in Semi-closed Communities**

A. H. GALE. *Lancet* [Lancet] 1, 735-741, March 31, 1951. 5 figs., 29 refs.

The author summarizes a number of epidemics of poliomyelitis occurring in closed communities between 1917 and 1949. These include 4 outbreaks in school camps, 4 in children's homes, the Broadstairs epidemic of 1926, and 31 outbreaks in boarding schools in England and the U.S. The author points out how difficult it is to trace any clear relationship between seasonal incidence, severity, and duration of an outbreak with the type of community involved. In camp outbreaks there seems to be a high incidence of paralytic cases; in children's homes a notable feature has been the high attack rate among staff. In schools there is at present no means of forecasting what is likely to happen when a paralytic case occurs, the difficulty being that in the early stages dissemination of the virus is at first a silent process. Multiple paralytic cases have rarely been encountered in schools for girls, and it is suggested that this may be due to the fact that girls are more likely to be confined to bed for comparatively trivial ailments than are boys. Outbreaks are certainly commonest in the autumn term, less so in the summer term, and very rare in the spring term, though they may occur at any period within a given term. The author stresses difficulties in the epidemiological study of poliomyelitis and points out the value of uniform methods of presenting clinical accounts of an outbreak. No new suggestion is made as to the best method of dealing with a localized outbreak, but once again the evil effects of exercise in the early stages of the disease are emphasized. In general the advice tendered by the Medical Officers of Schools Association in 1946 is regarded as the soundest at present available.

Joseph Ellison

**441. A Milkborne Poliomyelitis Episode**

M. LIPARI. *New York State Journal of Medicine* [N.Y. St. J. Med.] 51, 362-369, Feb., 1951. 4 figs., 4 refs.

The author describes an epidemic of poliomyelitis which occurred in Delaware County, N.Y., during late October, 1949. At this time poliomyelitis was not prevalent in the district, only 10 cases having been reported during the summer, one from the area under review. From September 26 to November 20 a total of 23 cases were reported from a locality with a population of 3,000 persons. During the same period 9 cases occurred in the rest of the county. Much evidence is collected to show that the outbreak was disseminated from a single dairy where the sole operator was the father of one of the patients. It was not, however, possible to prove that infected milk was the sole cause of spread in this epidemic, though it seems clear that its importance was paramount. Exceptionally high temperatures for the time of year are regarded as one important factor in fomenting this outbreak.

Joseph Ellison

**442. Homologous Serum Jaundice. An Occupational Hazard to Medical Personnel**

M. L. TRUMBULL and D. J. GREINER. *Journal of the American Medical Association* [J. Amer. med. Ass.] **145**, 965-967, March 31, 1951. 11 refs.

Attention is drawn to homologous serum hepatitis as a possible occupational hazard to all medical employees whose duties expose them to infected blood. The authors report 16 cases, mostly in one hospital, among blood-bank workers. No other cases were reported in other hospital departments during the same period. Others have noted 44 cases in hospital staffs, mostly laboratory workers, having a similar degree and character of exposure.

The diagnosis in the reported cases was based on: (1) the clinical picture; (2) a common factor of probable exposure to infected blood with some noted accidental inoculations; and (3) the incubation period in 2 of the cases. Recommendations as to strict adherence to the rules of asepsis are given, including the wearing of gloves to avoid contact with blood.

The authors believe that since these cases are occupational in origin the patients should be compensated accordingly.

*I. Dunsford*

**443. Renal Function in Silicosis. (La funzionalità renale nei silicotici)**

G. SAITA and O. ZAVAGLIA. *Medicina del Lavoro* [Med. d. Lavoro] **42**, 41-48, Feb., 1951. 21 refs.

The authors studied the renal function of 20 patients aged 36 to 59 years who had silicosis. Patients with cardiac disease, hypertension, and other serious disease, or with a history of renal disease, were excluded from the series. Six of the patients included had active pulmonary tuberculosis with positive sputum. Albuminuria was found in 4 cases, lipoiduria in 20, reduced ability to excrete dilute urine in 10, and a slight rise in blood urea level in 8. The authors discuss 3 possible mechanisms to account for the changes in renal function: the co-existence with silicosis of cardiac insufficiency, the elimination of silica through the kidneys, and the damaging effect of free silica on the mesenchymal tissues. They quote histological studies said to demonstrate fibrotic changes in the spleen, liver, and kidneys in patients dying from silicosis, and conclude that it is these effects which are responsible for the changes in renal function.

*John Pemberton*

**444. The Health of Ferrous Foundry Workers**

H. HEIMANN. *Public Health Reports* [Publ. Hlth Rep., Wash.] **66**, 223-239, Feb. 23, 1951. 1 fig., bibliography.

The workers in 16 iron foundries in the State of Illinois were investigated for the purpose of determining whether their work had any adverse effect on their health, 1,937 men being examined. Attrition of the occlusal surfaces of the teeth was of greater frequency than in other industrial workers not exposed to hard gritty substances such as silica. The incidence of pulmonary tuberculosis was 0.7% of the white and 1.7% of non-white workers, which is similar to that in the general population. The silicotic x-ray opacities found

were classed as linear, granular, nodular, or conglomerate; 140 men, or 7.7%, showed ground-glass granular shadowing with obliteration of the linear markings; 28, or 1.5%, showed nodular shadowing (in 24 of these the nodules were small, while in 3 they exceeded one millimetre in size; in one case conglomerate shadows were also present). The ages of the 28 ranged from 45 to 73 years, 18 were grey-iron workers, while 10 were steel foundrymen. Of the 18 iron workers, 14 were moulders; of the 10 steel men, 9 were cleaners and finishers. It is suggested that for iron foundrymen moulders have a higher incidence of nodular silicosis, whereas for the steel workers the cleaners and finishers have the higher incidence. It generally required more than 14 years of exposure in the industry for the shadowing to appear.

*K. M. A. Perry*

**445. Pneumoconiosis and Silicosis. (Пневмокониоз и силикоз)**

N. A. VIGDORCHIK. *Гигиена и Санитария* [Gigiena] No. 1, 20-25, 1951.

Quartz dust ( $\text{SiO}_2$ ) produces diffuse or localized fibrosis of the lung tissue. It is still doubtful whether any dusts other than quartz can produce a similar fibrosis. In other words, are there, except for silicosis, any other forms of pneumoconiosis? The term pneumoconiosis is still not defined properly and this causes a lot of misunderstanding. For instance, Tibbs defines pneumoconiosis as "any morbid condition of the lungs caused by inhalation of dust". According to that definition any case of bronchitis, asthma, or bronchiolitis which may be caused by dust must also be regarded as a case of pneumoconiosis.

The author then proceeds to present evidence proving that dust which does not contain quartz affects the respiratory tract only as far down as the alveoli, and that the quartz dust, in addition to the above, can also produce a diffuse fibrosis in the perialveolar tissue—that is, in the connective tissue and the lymphatic network forming the stroma of the lung.

*H. W. Swann*

**446. Contamination of Cetrimide and Other Fluids with *Pseudomonas pyocyanea***

E. J. L. LOWBURY. *British Journal of Industrial Medicine* [Brit. J. industr. Med.] **8**, 22-25, Jan., 1951. 8 refs.

*Pseudomonas aeruginosa* was isolated from a large number of solutions commonly applied to wounds in hospital, for example, soap solution, 10% "dettol", calamine lotion, and 1% cetrimide solution. Evidence was obtained that the infection was essentially in the cork stoppers; a sample of the solution was not positive when a sample from the cork was negative. The solutions were found to be free from contamination after screw-capped bottles were used.

*Scott Thomson*

**447. A New Industrial Disease Called Hyperhidrosis Erythema Traumatica**

J. H. T. DAVIES. *British Journal of Industrial Medicine* [Brit. J. industr. Med.] **8**, 95, April, 1951. 3 figs.

## Anatomy and Histology

### 448. New Facts Concerning the Bronchial Arterial Circulation. (Données nouvelles sur la circulation dans les artères bronchiques)

M. LATARJET and P. JUTTIN. *Poumon [Poumon]* 7, 35-36, Jan., 1951.

This is the first of a series of papers describing the distribution of the bronchial arteries to the lungs and pleura, and is devoted to the methods used.

The material consisted of 125 human adult lungs, removed from the body soon after death. The arteries were injected by catheterizing their orifices as they leave the aorta. A few millilitres of warm isotonic saline containing a few drops of toluene was injected, followed by the injection mass. This consisted of 10% sealing wax in 75% alcohol with the addition of 2 g. of red lead [sic], and was injected slowly with the specimen immersed in a bath at 40° C.

After radiography in two planes, the specimens were immersed in formalin for 3 to 4 hours and dissected with a binocular loupe. Specimens were taken for histological examination from appropriate regions and stained with haematoxylin and eosin, and with Weigert and safranin for elastic fibres. *D. B. Moffat*

### 449. Anatomic Variations of the Orifice of the Human Coronary Sinus

H. K. HELLERSTEIN and J. L. ORBISON. *Circulation [Circulation]* 3, 514-523, April, 1951. 12 figs., 15 refs.

The authors have studied the valves of the coronary sinus and inferior vena cava, with particular reference to the difficulties encountered in coronary-sinus catheterization. They examined 150 formalin-fixed hearts, of which 24% were from cases of congestive heart failure, from subjects ranging in age from 24 to 84 years. The diameter of the coronary-sinus opening was measured by inserting a tapered glass rod, which was then measured with callipers. The height (from attached to free edge) of the valve was also measured, together with the width of the medial extremity of the valve of the inferior vena cava in the region of the coronary-sinus opening (Eustachian ridge).

Six main variations of the coronary-sinus valve were found: (1) absent in 14.7%; (2) small and crescentic in 38%; (3) covering the entire orifice of sinus in 30.7%; (4) fibrous bars in 5.3%; (5) threads and networks in 5.3%; (6) common valve of caval and sinus openings in 6%. The average diameter of the opening after retraction of the valve was 9.6 mm., with a standard deviation of 2.2 mm. The size was related to the type of valve present, the heart weight, and the presence of congestive heart failure. In 21.3% of cases the valve of the inferior vena cava was absent and the Eustachian ridge smooth and non-prominent. In 47.3% the ridge was firm and over 1.6 mm. high, and in 25.4% it was membranous and rather wide (from 1 to 8 mm.). The

remaining cases are accounted for by other variations which are described.

The variations in oxygen content of the blood obtained at different levels in the right atrium and ventricle are ascribed to the mixing effect of the various types of coronary-sinus valve. Catheterization of the coronary sinus should be possible in a maximum of 75% of cases and very unlikely in the remainder. *D. B. Moffat*

### 450. The Postnatal Structural Changes in the Intrapulmonary Arteries and Arterioles

W. H. CIVIN and J. E. EDWARDS. *Archives of Pathology [Arch. Path.]* 51, 192-200, Feb., 1951. 13 figs., 12 refs.

In the lungs the elastic arteries are 1.0 mm. in diameter or larger, with endothelium close to a thick elastic lamella. The larger the vessel the more elastic tissue it contains. The muscular arteries occur between the elastic arteries and the arterioles. Arterioles are 0.1 mm. in diameter or less and are composed of endothelium surrounded mainly by collagen. During the last trimester of pregnancy the foetal lung has a definite polygonal lobular pattern. The arteries of the foetal interlobular septa become the elastic arteries in the adult. In the foetus the lumina are patent. At birth and for a short time afterwards the lumen is about equal to the thickness of the wall; then it dilates and the internal elastic lamella becomes thicker, and at 6 months the vessels have the adult appearance with widely patent, oval lumina and equal distribution of elastic fibres throughout the media. The vessels increase in size up to 20 years of age. The muscular artery evolves from the intralobular artery of the foetus. During the last trimester the lumen is very narrow, but shortly after birth there is a steady increase both in lumen and in wall thickness, and at 6 months the lumen is broader than the wall. Between the fourth and sixth post-natal months the internal elastic lamina appears and from then onwards the arteries increase in size and by 2 years they have an internal and usually an external elastic lamina. Growth continues until 20 years.

Arterioles cannot definitely be identified before birth, but can be recognized at 1 month. They continue to enlarge and are fully developed by 20 years. Arterial intimal fibrosis appears in the second decade in the muscular arteries; in the third, elastic arteries also are involved. This continues, and in the fifth decade the muscular arteries and arterioles show collagen in the intima, and the elastic arteries symmetrical intimal fibrosis. By the sixth decade all the vessels are involved.

The vessels at the periphery of the lung of the stillborn foetus are open, but centrally they are shut down. Continuation of the resistance of muscular arteries may impede the pulmonary circulation and be a factor in stillbirth. *Peter Harvey*

## Physiology and Biochemistry

### 451. Observations on the Eosinophil Count in Man. A Proposed Test of Adrenal Cortical Function

B. FISHER and E. R. FISHER. *American Journal of the Medical Sciences [Amer. J. med. Sci.]* **221**, 121-132, Feb., 1951. 5 figs., 14 refs.

A study has been made of the behaviour of eosinophil cells in man with the object of determining the validity of the fall in eosinophil count after administration of adrenaline or ACTH as an indicator of adrenal function. Eosinophil counts were made, Hinkleman's solution being used as diluent stain. To establish normal eosinophil counts, 463 observations were made on 170 individuals. Wide scatter was found in resting values, only 50% of counts falling within the range of 100 to 250 per c.mm. found in normal subjects by Thorn. A large diurnal variation was found in individuals. Scatter diagrams are shown. On comparison, the total leucocyte and eosinophil counts showed no relationship.

After the injection of an adrenal cortical extract no consistent change in eosinophil count could be observed in 25 normal subjects. After injection of 0.3 mg. of adrenaline into 25 normal subjects there was a fall in 4 hours of 40% or more in 64% of the subjects, but a similar fall was also found in 23.5% of a control group. In 4 of the normal subjects there was a fall of less than 15% after adrenaline.

It is concluded that it is misleading to use fluctuations in the eosinophil count as a sensitive indicator of variations in activity of the adrenal cortex.

C. L. Cope

### 452. A Study of the Physiological Eosinophilia of Old Age. (Étude de l'éosinophilie physiologique des sujets âgés)

L. BINET and G. MATHÉ. *Presse Médicale [Pr. méd.]* **59**, 305-307, March 10, 1951. 40 refs.

In this investigation 50 patients over 60 years of age were grouped according to: (a) chronological age, (b) apparent age, and (c) functional state. Blood eosinophil levels were determined by the direct method. The eosinophil count could not be correlated with sex or "real" age, but was related to the "apparent" age and, more closely, to the "functional state"; lower eosinophil levels occurred in the more decrepit patients. [The "overlap" is considerable.] Sternal-marrow studies on 12 patients showed the blood eosinopenia to be associated with hypoplasia of the eosinophil series alone, other marrow cells being normal.

Adrenaline was used to test the pituitary-adrenocortical function of 37 patients. It was found that the fall in circulating eosinophils was greatest in those patients of least "apparent" age and of highest "functional state", but bore no relation to sex or "real" age; 10 patients were also tested with cortisone, but the results were equivocal.

The authors suggest that the low "functional state" of senile decrepitude derives, in part at least, from pituitary-adrenocortical hypofunction.

P. D. Bedford

### 453. Endocrine Control of the Adrenal Gland

J. D. FELDMAN. *Anatomical Record [Anat. Rec.]* **109**, 41-58, Jan., 1951. 37 refs.

Injection of ACTH into intact rats produces hypertrophy of the adrenal glands with loss of carbonyl-positive, lipid, and birefringent material from the cortex. Hypophysectomy also causes loss of these materials and cortical atrophy in addition. The administration of thyroxine to intact rats causes adrenal hypertrophy, while thyroidectomy produces atrophy. In hypophysectomized rats, thyroxine has no effect on the adrenal. Growth hormone causes no change in the adrenal visible either macroscopically or microscopically.

Norval Taylor

### 454. Urinary Excretion of Inorganic Phosphates. (L'excrétion urinaire des phosphates inorganiques)

E. JACOBS and P. P. LAMBERT. *Journal d'Urologie Médicale et Chirurgicale [J. Urol. méd. chir.]* **56**, 737-754, 1950. 4 figs., 17 refs.

The urinary excretion of inorganic phosphate after intravenous injection of phosphate buffer at pH 7.4 was studied in 15 normal subjects. The blood phosphate level reached 150 mg. per l. in 5 of the subjects, but in the other 10 did not exceed 105 mg. per l. by the time the first urinary collection was made at 20 to 25 minutes after injection. Glomerular filtration rates were determined with mannitol, and the amounts of inorganic phosphate filtered and reabsorbed per minute were calculated on the assumption that all plasma inorganic phosphate is filtrable.

The reabsorption of phosphate at first rises with the blood phosphate level, but becomes constant when the level exceeds 60 to 70 mg. per l. However, this relationship is not followed at blood phosphate levels above 105 to 110 mg. per l., and at these concentrations it appears as if the tubules again absorb increasing quantities of phosphate. This result cannot easily be explained unless it is postulated that a non-filtrable colloidal calcium phosphate is formed in the plasma at phosphate levels greater than 100 mg. per l. This hypothesis is confirmed by a series of previous observations which, the authors claim, tend to prove the appearance of such a complex in plasma when the calcium  $\times$  phosphate product exceeds 100; if this is indeed the case, the non-filtrable phosphate would be added to that reabsorbed by the tubules.

In the 10 subjects with blood phosphate levels of less than 105 mg. per l. the mean value of the ratio of glomerular filtration rate after phosphate to mannitol

clearance was  $1.11 (\pm 0.09)$ ; the mean value of this ratio in those with higher plasma phosphate levels was  $0.74 (\pm 0.088)$ . This is an absurd result, yet the difference between the two means is statistically significant and there are only 3 chances in 100 that it could be due to chance. The authors claim that these observations provide decisive evidence in favour of the hypothesis that the formation of a colloidal phosphate at very high blood phosphate levels masks the saturation of tubular reabsorption of phosphate.

R. P. Hullin

#### 455. Positive Acceleration and Urine Output

F. R. STAUFFER and E. O. ERREBO-KNUDSEN. *Journal of Aviation Medicine [J. Aviat. Med.]* 21, 500-506 and 525, Dec., 1950. 2 figs., 16 refs.

The effect of acceleration on urine output was studied in 10 adult males. During the control experiments each subject was seated and drank 100 ml. of tap water every 10 minutes. The bladder was emptied every 10 to 20 minutes: the first urine specimen was discarded, and the volume and specific gravity of the subsequent samples were determined. Exposure of subjects "water-loaded" in this way to accelerations of  $+3 g$  for one minute caused a reduction in urinary output and increase in the specific gravity of the urine. On exposure to  $+5 g$  for one minute, an "anti-g suit" being worn, these changes were greater and lasted longer. Changes in renal blood flow and tubular reabsorption are considered as possible explanations of these findings.

D. H. Sproull

#### 456. Factors Maintaining Cerebral Circulation during Gravitational Stress

J. P. HENRY, O. H. GAUER, S. S. KETY, and K. KRAMER. *Journal of Clinical Investigation [J. clin. Invest.]* 30, 292-300, March, 1951. 4 figs., 32 refs.

The subjects of these experiments were exposed to accelerations of  $+1.0$  to  $+4.5 g$  in the "human centrifuge". Arterial pressure was measured by a strain gauge connected with a cannula in the radial artery, the wrist being held at head level, and the internal jugular venous pressure was also measured by a strain gauge. Samples of blood were taken for measurement of the oxygen content by the van Slyke manometric method. In two subjects the oxygen content of the jugular vein was measured directly with a Kramer oximeter.

It was found that although consciousness is usually lost when the mean cerebral blood pressure falls to 25 mm. Hg, during exposure to high accelerations consciousness may be retained in spite of such a reduction. In three subjects the arterial and cerebral venous oxygen saturations were determined during acceleration: the venous saturation was almost unchanged, suggesting some mechanism for maintaining the cerebral blood flow. Pressures from 20 to 60 mm. Hg below normal were found in the jugular bulb. It is suggested that the cerebral blood flow could be maintained by sustaining the arterio-venous pressure differential, or by combining such an effect with passive cerebral vasodilatation.

D. H. Sproull

#### CIRCULATORY SYSTEM

457. The Role of the Lungs as a Blood Depot in Regulation of the Circulation under Normal and Pathological Conditions. (Betydelsen av lungornas bloddepåfunktion för blodcirkulationens regulation under normala och patologiska förhållanden)

T. SJÖSTRAND. *Nordisk Medicin [Nord. Med.]* 45, 159-164, Jan. 31, 1951. 4 figs., 26 refs.

In this paper the author draws conclusions from his work on the distribution of blood in animals and man following changes of posture, activity, and environmental temperature (*Skand. Arch. Physiol.*, 1934, 71, 85). He suggests that earlier work carried out on animals may have exaggerated the importance of the effect of the filling of the right heart on the cardiac output, while the balancing effect of the lungs was overlooked. He considers that filling of the left ventricle is an important factor in the regulation of the cardiac output, and that the pulmonary blood vessels act "like a dam in a hydro-electric plant". He considers, moreover, that the blood vessels of the lungs play an active part both in the maintenance of a high cardiac output during exercise and in compensating for a low cardiac output in [certain cases of] heart failure, and that by varying the diastolic filling of the left side of the heart, the lungs are able to influence the heart rate after changes of posture or treatment of heart failure with digitalis.

[See also *On the Principles for the Distribution of the Blood in the Peripheral Vascular System*, Berlin, 1935, and *Acta physiol. scand.*, 1941, 3, 49.]

E. M. Glaser

#### 458. A Comparison of Coronary Flow Determined by the Nitrous Oxide Method and by a Direct Method Using the Rotameter

D. E. GREGG, F. H. LONGINO, P. A. GREEN, and L. J. CZERWONKA. *Circulation [Circulation]* 3, 89-94, Jan., 1951. 1 fig., 8 refs.

Considerable differences occur in the results obtained by the two methods, and the degree of difference varies under different haemodynamic states. Despite a multiplicity of possible errors in the nitrous oxide method, the authors hold that it can give a useful measure of the amount of coronary arterial blood flow.

Albert Venner

459. Variations in Blood-pressure Readings in Healthy Students who were Subjected to Emotional Stress or Cold. (Колебания кровяного давления под влиянием эмоциональных факторов и холодовой пробы у здоровых лиц)

G. L. KAZ. Клиническая Медицина [*Klin. Med. Mosk.*] 28, No. 12, 74, 1950.

Blood-pressure readings were taken on 192 healthy medical students who were about to sit for their final examination. The first reading was taken at rest, the second 30 minutes before the examination, the third 30 minutes after the examination. During the first test 12 students showed a raised blood pressure [but no figures are given]. In the second test 51 students

showed raised systolic and diastolic pressures, 23 a raised systolic, and 31 a raised diastolic pressure. In most cases the systolic pressure was raised 30 to 40 mm. Hg, in 9 cases 50 mm. Hg, and in one case 60 mm. Hg. The diastolic pressure was raised about 20 mm. Hg in most cases. It is thought by the author that the systolic blood pressure is the more sensitive towards emotional factors. In 19 students the blood pressure remained raised at the third test, it having returned to the resting level in the remainder.

Blood pressure was recorded during rest in 140 healthy students aged 22 to 25 years. The readings were taken every 5 minutes until a stable level was reached. The other arm was then submerged in cold water and the blood pressure was taken after 30 seconds and 60 seconds. Thirteen students showed a systolic and diastolic rise of about 20 mm. Hg each, and 32 showed a diastolic rise only. It is suggested that the diastolic blood pressure is the more sensitive towards cold.

*N. Chatelain*

#### 460. Effect of Venous Occlusion on Peripheral Arterial Blood-flow

J. E. THOMPSON and J. R. VANE. *Lancet* [Lancet] 1, 380-382, Feb. 17, 1951. 4 figs., 15 refs.

Intermittent venous occlusion has been employed in the treatment of obliterative disease of the blood vessels, the basic idea being that hyperaemia may follow the release of the occlusion and permit an improved collateral circulation. In view of conflicting reports as to the results of this treatment a detailed study of the problem was made in cats. In experimental animals direct measurements were usually made of the arterial blood flow during and after periods of venous occlusion, while in man indirect methods were employed.

In animal experiments the leg artery was perfused, and the rate of blood flow and perfusion pressure directly measured. The actual volume of blood entering the leg alone could in this way be recorded. Intermittent venous obstruction was carried out on the limbs, but the reactive hyperaemia did not last longer than 20 or 30 seconds and did not compensate for the reduced flow occurring during occlusion. Thorotrast and radiography were also used in studying the volume of vessels.

It is concluded that venous occlusion actually decreases the arterial inflow, and that any transient increase in arterial flow following release of the venous obstruction does not compensate for the reduction during the period of occlusion. The possible errors which gave rise to the impression that there was an increased arterial supply are described.

*T. Holmes Sellors*

#### 461. Observations on the Frequency of Blood Groups A, B, O, and Rh in Greece. (Quelques observations sur la fréquence des groupes A, B, O et Rh en Grèce)

G. E. PANGALOS, M. PAVLATOU, and M. ROUSSOU. *Sang* [Sang] 22, 153-154, 1951.

The rarity of Rh-negative blood in Greece (9.9%) is attributed to the admixture of oriental races, among which Rh negativity is very rare.

*A. Piney*

#### 462. Haemopoiesis and Siderosis in the Foetus and Newborn

F. A. LANGLEY. *Archives of Disease in Childhood* [Arch. Dis. Childh.] 26, 64-75, Feb., 1951. 4 figs., 44 refs.

A study was made of the amount of erythropoietic tissue and stainable free iron in the organs of the newborn; the results are described, and form the basis of a reconsideration of the changes in the haematopoietic system at birth. Sections of liver, spleen, and kidney were examined from 92 infants, 18 of whom were stillborn and 74 ranged in age at death from 10 minutes to 7 months. Of the total, 48 were premature and 44 full-term infants. In none was there evidence of haemolytic disease. The limits of prematurity were 38 weeks' gestation and 48 cm. crown-heel measurement. Among stillborn infants the mean content of haematopoietic foci in the liver was clearly greater in the premature group, though no relationship emerged between amount of haematopoietic tissue and the degree of prematurity. Prenatal recession of erythrocyte production occurred in the 38th and 40th weeks.

In the liveborn group a process of postnatal recession began at 2 to 3 days of age and was complete about the eighth day in full-term infants, but was prolonged by prematurity, according to its degree, up to 38 days' duration. This period was considerably less than the number of days of prematurity. Postnatal recession differs from the foetal type, and closely follows a logarithmic law. Visible iron pigment was present in the liver in two-thirds of the cases, including half of the stillborn group. No correlation was found between siderosis and prematurity, but siderosis and haemopoiesis occurred more often apart than together. Siderosis was rarely present between the first and third days, increased to the fourth week, and decreased after 3 months. Incidence in the spleen followed that in the liver; there was a positive reaction to iron in only 2 instances in the kidney.

The postnatal fall in the erythrocyte count in the second week of life and the physiological jaundice of the newborn have been attributed to haemolysis. The author regards the former change as reflecting the diminishing haematopoietic function of the liver; the iron supplied for this activity accumulates as less is used, and some is deposited in the spleen. The latter condition may result from immaturity of liver function.

More extensive knowledge of such factors as changes in blood volume at birth, rate of production of both liver and marrow erythrocytes, and their attributes is required before the part, if any, played by haemolysis can be assessed.

*V. Reade*

#### 463. The Desoxyribose Nucleic Acid Content of the Resting Nuclei of the Normal Myeloid Cells of Man. (Sur la teneur en acide désoxyribonucléique des noyaux au repos des cellules myéloïdes normales chez l'homme)

G. MARINONE. *Sang* [Sang] 22, 89-98, 1951. 3 figs., 10 refs.

Maturation of myeloid cells is accompanied by a sudden decrease in desoxyribose nucleic acid content at two different stages of cellular development. The first

reduction coincides with the disappearance of nucleoli; the second with loss of the power of cell division. The mechanism of the decrease is still obscure.

[This stimulating paper should be read in conjunction with that of Pearse, *J. clin. Path.*, 1951, 4, 1.]

A. Piney

## NUTRITION AND METABOLISM

### 464. Absorption Studies using Portal Anastomotic Veins

W. B. BEAN, M. FRANKLIN, J. F. EMBICK, and K. DAUM. *Journal of Clinical Investigation* [*J. clin. Invest.*] 30, 263-273, March, 1951. 10 figs., 23 refs.

The authors studied the absorption, by 2 patients with cirrhosis of the liver, of a test meal containing protein, fat, glucose, fructose, and vitamins A, B, and C. Biochemical determinations were made on blood samples collected simultaneously from an antecubital vein (systemic blood) and a portal anastomotic vein on the abdominal wall (portal blood). The results of these analyses are presented in a series of charts, together with the circulation time, portal-vein pressure, and oxygen saturation of the blood. The application of such methods to the investigation of portal circulation and hepatic metabolism is discussed, the limitations being fully realized.

A. I. Suchett-Kaye

### 465. Observations of Normal and Abnormal Human Intestinal Motor Function

E. L. POSEY and J. A. BARGEN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] 221, 10-20, Jan., 1951. 5 figs., 15 refs.

At the Mayo Clinic, Rochester, Minnesota, the authors recorded the intestinal movements of 24 patients with ileal or colonic stoma (or both) by means of two balloons (the " tandem-balloon technique "). The subjects were suffering from a variety of intestinal disorders, traumatic, inflammatory, and neoplastic.

Templeton and Lawson (*Amer. J. physiol.*, 1931, 96, 667), described three types of intestinal wave in the dog's bowel. Type-I waves are " small, frequent pulsations, rhythmical and non-propulsive "; Type II are " larger, slower and potentially propulsive "; Type-III waves " are tonus waves surmounted by Type I or Type II patterns, propulsion, when achieved, is by virtue of the Type II configuration ". In general the results obtained in this study confirm these findings.

The human intestine normally showed different types of activity at the site of each balloon. By varying the distance between pairs of balloons it was concluded that in the small intestine the functional unit was about 4 cm. long, and in the large bowel about 6 cm. long. Transport of material from proximal to distal segment was not observed unless two adjacent units showed activity of the propulsive type together. More distantly related segments, however, normally show different types of activity. This normal incoordination is considered to act as a brake on the rapid passage of intestinal contents;

the excessive segmental coordination in ulcerative colitis probably accounts for the diarrhoea observed in that disease. Incoordination between bowel segments, if excessive, produced abdominal discomfort. It is considered that this excess incoordination is responsible for the abdominal symptoms usually attributed to " spasm ", despite the fact that no such dyssynergia was recorded in the two cases of ulcerative colitis investigated—the possible explanation of this anomaly in a disease associated with much abdominal " cramp " is discussed. In view of this conclusion it is suggested that the rationale of the drugs at present regarded as anti-spasmodics be questioned. It is also considered that excessive or defective tone may inhibit motility. No change in motility was noted during sleep; retrograde transport was observed, and unused segments of bowel were found to be capable of normal motility.

A. T. Macqueen

### 466. The Metabolism of Iron during Suckling

R. A. McCANCE and E. M. WIDDOWSON. *Journal of Physiology* [*J. Physiol., Lond.*] 112, 450-458, Feb. 20, 1951. 1 fig., 25 refs.

The total amount of iron in the bodies of mice, rats, kittens, and piglets increased during suckling. The piglets obtain this additional iron from their surroundings, the other species from their mother's milk. The liver of rabbits contains large amounts of iron at birth; this iron is not withdrawn during suckling and the animals become anaemic, as little iron is absorbed from the intestines. The iron content of the liver falls in the suckling period, partly due to liver growth; except in the rabbit, the liver iron at birth is only a small fraction of the whole body iron. The percentage of iron in the blood of kittens and piglets fell during growth, and the percentage of iron in the extravascular and extrahepatic tissues increased. It is calculated that in human infants the body iron should increase by 40% in the suckling period, the iron being provided in the mother's milk.

A. Schweitzer

### 467. Proof of the Early Utilization of Fat Administered Intravenously into Human Subjects

B. G. P. SHAFIROFF, J. H. MULLHOLLAND, and J. BAKER. *Experimental Medicine and Surgery* [*Exp. Med. Surg.*] 9, 184-188, Feb., 1951. 1 fig., 5 refs.

Tristearic acid was prepared containing deuterium (5 atoms %). A 10% fat emulsion was made from equal volumes of this and of coconut oil, together with gelatin, glucose, and a mixture of amino-acids. Three subjects were each infused with one litre of the emulsion, and samples of blood, urine, and expired air were taken at intervals over 24 hours. Oxygen consumption increased during the infusion and remained high for about 12 hours. Analysis of the water in the expired air and of the urine showed a rapid elimination of deuterium, indicating that about 50% of the labelled fat was metabolized within 24 hours. The remainder was presumably converted into phospholipids and deposited in the fat depots. These experiments show that human subjects are able rapidly to oxidize part of the fat in an emulsion given intravenously.

John Yudkin

468. The Serum-protein Levels of Samoans, Fijians, and Indians in Fiji

L. WILLS and M. E. BELL. *Lancet [Lancet]* 1, 820-822, April 14, 1951. 21 refs.

469. Sequelae to the Administration of Vitamin B<sub>12</sub> to Humans

B. F. CHOW. *Journal of Nutrition [J. Nutrit.]* 43, 323-343, Feb., 1951. 3 figs., 13 refs.

This paper gives the results of preliminary experiments upon the metabolism and effects of vitamin B<sub>12</sub> in human subjects. Oral administration of up to 5 mg. in a single dose or 25 µg. daily for several months did not result in an increased urinary excretion. More than half of the larger doses could be recovered from the faeces. It seems, therefore, that only small, but apparently adequate, amounts are absorbed from the alimentary canal. Intravenous administration led to an increased urinary excretion. In the blood the vitamin appears to circulate only in the plasma; there was no evidence of penetration into, or adsorption on to, the erythrocytes.

The effect on nitrogen retention was studied in 4 infants of 3 to 6 months fed on a soy-bean preparation. Intramuscular injection of vitamin B<sub>12</sub> had no effect on nitrogen retention; this supports the suggestion which has been made that the vitamin probably affects carbohydrate or fat metabolism rather than protein metabolism.

Experiments were also conducted to examine suggestions that vitamin B<sub>12</sub> by mouth affected the growth of children. One such study was with 45 children suffering from a variety of chronic diseases. Those over 2 years of age received 25 µg. daily, and those under 2 years received 10 µg. After 3 months there was a significantly greater gain in weight in the treated group of 24 children than in the untreated group of 21. Similar results were obtained with 18 normal boys of 18 to 47 months, 9 of whom received 25 µg. daily for 6 months. It is stressed that owing to various differences between the treated and control groups in both of these studies the results must be regarded as suggestive rather than as definite proof of the effect of vitamin B<sub>12</sub> on the growth of children.

John Yudkin

470. Vitamin B<sub>12</sub>, a Factor in Prevention of Hydrocephalus in Infant Rats

B. L. O'DELL, J. R. WHITELEY, and A. G. HOGAN. *Proceedings of the Society for Experimental Biology and Medicine [Proc. Soc. exp. Biol., N.Y.]* 76, 349-353, Feb., 1951. 1 fig., 6 refs.

It was found some years ago that feeding rats on a synthetic diet containing casein as the only source of protein causes hydrocephalus in about 2% of the offspring. The present authors have shown earlier that this is due to a nutritional deficiency and that it could be prevented by the addition of aqueous liver extract, and in some instances also by addition of folic acid, to the diet. They observed an increase in the incidence of hydrocephalus up to 20% in the offspring when a folic acid inhibitor, crude methylpteroylglutamic acid (methyl P.G.A.), was added to a diet that contained soy-bean oil meal as the source of protein. The type of diet consumed during

the pre-experimental period had a marked effect on the incidence, and this suggests that the protective factor may be stored in the mother rats.

To test the importance of vitamin B<sub>12</sub> 3 groups of rats were used. Group I was maintained on a basal diet free of vitamin B<sub>12</sub> for at least 3 months in order to deplete them of the protective factor. Afterwards, during the experimental period, the animals received the same diet, to which crude methyl P.G.A. was added. Group II was not depleted but received the same diet as Group I. Group III was also not depleted, but received vitamin-B<sub>12</sub> concentrate in addition to methyl P.G.A. in the diet. The incidence of hydrocephalus was 23% in the offspring of Group I, 15% in Group II. The same difference was seen in the second litters, but after the third litter there was very little difference. In Group III (vitamin B<sub>12</sub> added) no hydrocephalus was observed among the 1,261 offspring. In order to verify that vitamin B<sub>12</sub> was responsible for this protection, and not some other factor in the concentrate, crystalline vitamin B<sub>12</sub> was injected into 5 female rats that had produced at least 3 consecutive litters with hydrocephalus. No hydrocephalic offspring were observed. Efforts were made to determine when vitamin B<sub>12</sub> had to be injected in order to prevent the abnormality; the damage occurred after the seventh day of gestation, probably about the twelfth to fourteenth days.

Addition of folic acid in the absence of vitamin B<sub>12</sub> did not prevent the abnormality.

Z. A. Leitner

471. Nutritional Factors in Hemodynamics: Dissociation of Pressor Response and Hemorrhage Resistance in Avitaminosis C

R. E. LEE and E. A. HOLZE. *Proceedings of the Society for Experimental Biology and Medicine [Proc. Soc. exp. Biol., N.Y.]* 76, 325-329, Feb., 1951. 2 figs., 10 refs.

Direct microscopy of the mesentery of guinea-pigs lacking ascorbic acid revealed not only a slowing of the blood flow and increased fragility of the venules, but also a reduced reactivity of the terminal arterioles to adrenaline. In the larger, more proximal, arterioles, however, ascorbic acid deprivation did not affect the constrictor response to adrenaline.

Compared with pair-fed controls, guinea-pigs on a scorbutic diet showed a reduced survival time, a decreased resistance to anaesthesia, and a diminished ability to withstand comparable amounts of blood-loss. It is conceivable that these observations are related to the apparent dissociation between acute pressor effect and resistance to haemorrhage in ascorbic acid deficiency. It is suggested that the function of the larger arterioles with undiminished constrictor response to adrenaline in such conditions primarily consists of maintaining the normal tension and of producing the vasoconstrictor component of acute pressor reactions. The smaller terminal arterioles, on the other hand, with greatly reduced constrictor response to adrenaline in ascorbic acid deficiency, may act chiefly by supplementing the pressor mechanism of the larger vessels in acute stress and during more sustained attempts at blood-pressure elevation.

Z. A. Leitner

## Pharmacology and Therapeutics

### 472. Psychotic Reactions during Tetraethylthiuram-disulfide (Antabuse) Therapy

A. E. BENNETT, L. G. MCKEEVER, and R. E. TURK. *Journal of the American Medical Association* [J. Amer. Med. Ass.] **145**, 483-484, Feb. 17, 1951. 6 refs.

Of 37 patients treated with "antabus" 6 had transient psychotic reactions soon after beginning treatment. In 4 the symptoms developed while the drug alone was given, in the other 2 they came on after the ingestion of alcohol following about 2 months of drug treatment. In all cases symptoms subsided after administration of the drug was stopped. Except in 2 cases in which there was a paranoid element, the psychotic reactions did not resemble those of alcoholism. Five patients had evidence of liver damage and 4 of organic brain damage before treatment. Experimental work has shown that *in vitro* antabuse considerably reduces the oxygen consumption of nervous tissue. This suggests that the drug may interfere with the metabolism of an already damaged brain sufficiently to precipitate an organic psychotic reaction.

The authors have now reduced their dosage of antabus and in 50 recent cases there have been no psychotic reactions.

Marianna Clark

### 473. Mechanism of the Action of Tetraethylthiuram Disulfide in Alcoholism. Iron as Antidote for the TETD-Alcohol Reaction

J. A. CHRISTENSEN. *Quarterly Journal of Studies on Alcohol* [Quart. J. Stud. Alcohol] **12**, 30-39, March, 1951. 18 refs.

The toxic reactions to alcohol in subjects given tetraethylthiuram disulphide (TETD), also known as "antabus", include vasodilatation, tachycardia, tachypnoea, and an initial rise in blood pressure followed by a prolonged fall. They are believed to be due to an increase in blood acetaldehyde brought about by inhibition of liver aldehyde oxidase. However, small doses of intravenous iron, with or without ascorbic acid, will counteract these effects without altering the level of acetaldehyde in the blood. Since acetaldehyde is known to be a potent sympathomimetic drug it was decided to compare its effect on the blood pressure of dogs with that of adrenaline. Its action was found to be identical with that of a dose of adrenaline 1,000 times weaker, each causing a rise in blood pressure with return to normal in 6 to 7 minutes, and the initial rise in blood pressure being abolished by "C-7337", an adrenergic blocking agent. When TETD had been given, the initial rise in pressure occurred with each drug as before, but recovery was delayed for 20 to 35 minutes. The addition of small amounts of iron resulted in a return to normal levels in 6 to 7 minutes as in the first experiment.

It is clear that TETD increases the sensitivity of certain adrenergic receptors to acetaldehyde (and adrenaline), thus producing the symptoms seen after ingestion of alcohol; the effect can rapidly be neutralized by iron, which probably forms a complex salt with TETD. The apparent lack of correlation between blood acetaldehyde levels and toxic symptoms is in this way resolved.

A. Paton

### 474. The Effect of Tetraethylthiuram Disulfide on the Metabolism of Ethyl Alcohol

H. W. NEWMAN and H. V. PETZOLD. *Quarterly Journal of Studies on Alcohol* [Quart. J. Stud. Alcohol] **12**, 40-45, March, 1951. 9 refs.

It is not yet clear why tetraethylthiuram disulphide (TETD), also known as "antabus", raises the blood acetaldehyde level in subjects given ethyl alcohol. Experiments were therefore undertaken on dogs, which approximate nearest to man in their metabolism of alcohol, to determine: (1) what effect TETD has on the rate of disappearance of alcohol from the blood; and (2) what is its action on acetaldehyde metabolism. Alcohol or acetaldehyde was given intravenously, and TETD by mouth, to 6 animals. The results were clear-cut. First, there was no increase in the rate of alcohol metabolism, as determined by the fall in blood level, after TETD. Second, there was a significant rise in blood acetaldehyde levels when both alcohol and TETD were given. Third, the blood level after slow infusion of acetaldehyde was higher in animals receiving TETD than in controls. Thus TETD does not increase the metabolism of alcohol, as was originally believed, but apparently delays the rate of acetaldehyde destruction. Some dogs, like some men, are resistant to its action.

A. Paton

### 475. On the Effect of Trypan Blue and Congo Red on the Heart and the Blood Vessels. (Über den Einfluss von Trypanblau und Kongorot auf das Herz und die Blutgefäße des Frosches)

E. MIETKIEWSKI. *International Archives of Allergy and Applied Immunology* [Int. Arch. Allergy] **1**, 274-284, 1951. 2 figs., 8 refs.

Whereas trypan blue and Congo red caused shock-like symptoms in dogs when injected intravenously, they had no toxic effect on the heart and blood vessels of the frog.

K. Maunsell

### 476. The Liver in Shock Due to Dyes. (Die Leber im Farbstoffschock)

E. CZARNECKI, J. KIERSZ, and E. MIETKIEWSKI. *International Archives of Allergy and Applied Immunology* [Int. Arch. Allergy] **1**, 285-291, 1951. 5 figs., 8 refs.

In dogs a single intravenous injection of trypan blue caused symptoms similar to anaphylactic shock. The fall in blood pressure was marked. Intravenous

injection of this dye following ligation of the mesenteric arteries, hepatic artery, and hepatic vein had no shock-like effect. The blood pressure remained constant or showed a slight rise. The authors assume that the substances responsible for the dye-shock were liberated in the liver.

K. Maunsell

**477. The Inhibition of Testicular Hyaluronidase by Heavy Metals**

K. MEYER and M. M. RAPPOR. *Journal of Biological Chemistry* [J. biol. Chem.] **188**, 485-490, Feb., 1951. 1 fig., 10 refs.

Ferric, cupric, ferrous, and zinc salts were found to inhibit testicular hyaluronidase, this property decreasing in the order mentioned. Other metals including cadmium, lead, and mercury were found inactive. The inhibition could be prevented or reversed by a number of metal complex formers. When  $Fe^{+++}$  was used as the metal inhibitor, pyrophosphate was found the most potent reversing agent, while with  $Cu^{++}$  cysteine was most active. Potent chelating agents such as oxine, ethylenediamine-tetra-acetic acid, and dithione were rather poor competitors with the enzyme for the metal. The group or groups in the enzyme binding the metal are not known; SH groups appear to be excluded by the failure of *p*-chloromercuribenzoic acid to inhibit the enzyme.—[Authors' summary.]

**478. Development of Tolerance of Skin towards Antihistaminic Drugs**

S. MONASH. *Urologic and Cutaneous Review* [Urol. cutan. Rev.] **54**, 723-726, Dec., 1950. 9 refs.

By introducing a standard dose of known dilutions of histamine into the skin by iontophoresis the threshold for the individual tested can be obtained. The threshold is the dilution at which skin whealing first appears. All solutions used must be fresh, as they deteriorate quickly. The effect on this threshold value of various antihistaminic substances can be then tested. In 10 out of 11 cases previous administration of small doses of diphenhydramine, tripeleannamine, or "chlortrimeton" for a week only resulted in a refractory state of the skin, or tolerance to these drugs. This would explain the occasional development of urticaria in the skin of patients receiving diphenhydramine.

F. B. Cockett

**479. The Cardiovascular Effects of Some Narcotics. [In English]**

R. A. HUGGINS, W. G. GLASS, and A. R. BRYAN. *Archives Internationales de Pharmacodynamie et de Thérapie* [Arch. int. Pharmacodyn.] **86**, 112-120, March, 1951. 3 figs., 16 refs.

The action of morphine and of several synthetic morphine substitutes on the cardiovascular system of dogs was studied in respect of total peripheral resistance, blood pressure, and cardiac output. In small intravenous doses morphine, codeine, pethidine, "methadon", "metapon", and papaverine caused immediate vaso-dilatation by direct action on peripheral vessels. The fall in total peripheral resistance caused a fall in blood

pressure, unless this was prevented by a sufficient rise in cardiac output. Although the cardiac output rose with all the drugs named, it prevented a fall in blood pressure only with metapon, methadon, and papaverine. "Dilauid" was the only drug tested that caused an increase in total peripheral resistance.

When these drugs were given by the carotid artery their effects were similar but enhanced. This suggested that their peripheral action was augmented by a direct action on the vasomotor centre. Dilauid was again an exception in this respect, for when injected into the carotid artery this drug lowered the peripheral resistance and increased the cardiac output.

With large doses (at a therapeutically dangerous or even lethal level) the effects were all much greater and more prolonged. Recovery of blood pressure depended upon a rise in cardiac output. With codeine the cardiac output failed to rise and the blood pressure remained low throughout the period of observation (15 minutes). The compensatory mechanism was most successful with methadon and papaverine.

The anaesthetic used, soluble barbitone, undoubtedly modified the action of several, if not all, of these drugs.

*n*-Allylnormorphine, which protects the respiratory centre from the depressive action of morphine, also protected an animal from twice the lethal dose of methadon. It did not appear to influence the characteristic fall in total peripheral resistance.

Paul Wood

**480. Salicylamide: Pharmacology, Fate and Clinical Use**

M. LITTER, A. RUIZ MORENO, and L. DONIN. *Journal of Pharmacology and Experimental Therapeutics* [J. Pharmacol.] **101**, 119-124, Feb., 1951. 4 figs., 5 refs.

In view of the undesirable side-reactions that often limit the use of the salicylates it was decided to investigate further the effect of salicylamide on laboratory animals in preparation for a clinical trial of the drug in acute rheumatism and other types of arthritis. Depression of the central nervous system and paralysis were produced in guinea-pigs, rabbits, dogs, cats, and mice by a dose of 0.1 to 0.25 g. per kg., double this dose caused narcosis lasting for 1 to 2 hours, while doses of 1.0 to 2.0 g. per kg. resulted in death from respiratory paralysis. The amide was given by the oral, intraperitoneal, or intravenous route. Hypotension observed in the effective dose range was the result of peripheral vasodilatation and not of depression of the heart, which, however, occurred after very high doses. In mice the LD<sub>50</sub> was 0.313 g. per kg. These observations led the authors to the conclusion that salicylamide is a depressant, whereas the salicylates are more or less stimulant.

By determination of the minimum quantity of salicylamide necessary for analgesia in 90 rheumatic patients it was decided that the average effective and safe dosage was 2 g. every 4 to 8 hours day and night. The results of a trial on 118 patients suffering from a variety of rheumatic conditions showed that there was a marked analgesic effect in 50.8%, a moderate effect in 25.4%, a doubtful effect in 6.8% of cases, while 17% of patients had no relief. Of 7 patients with rheumatic fever, in

6 marked relief from pain was noted. The prothrombin time was shortened by salicylamide, whereas with salicylate administration it is lengthened. The toxic symptoms were dizziness in 22%, drowsiness in 7.6%, nausea in 5.9%, and heartburn in 3.4%; anorexia and diarrhoea each affected one patient. Excretion studies were attempted, but difficulties in the analysis of salicylamide were encountered, as the amide does not hydrolyse readily. It was concluded that salicylamide is useful in rheumatoid conditions and is better tolerated than salicylates.

R. Hodgkinson

**481. The Effect of Digitoxin on the Apparent Stroke Volume, Posteroanterior Cardiac Diameter, and the Cardiac Cycle in Normal Subjects as Studied by the Electrocardiograph**

E. E. EDDLEMAN, K. WILLIS, M. J. GREVE, and H. E. HEYER. *American Heart Journal [Amer. Heart J.]* 41, 161-181, Feb., 1951. 4 figs., 33 refs.

The apparent stroke volume and minute cardiac output were calculated from electrocardiographic observations made on 12 normal subjects. The subjects pursued their normal activities, but sat motionless for 15 minutes before observations were made.

On the first day control observations were made before each of the three main meals. On the second day digitoxin (1.0 mg., 0.6 mg., and 0.4 mg. respectively) was given immediately after each observation. Observations were made on each successive morning until normal levels were again reached. The cardiac output fell in 2 subjects in the first 4 hours and rose again after 36 to 48 hours. In 5 subjects a transitory fall in cardiac output after 4 hours was succeeded by a second fall after 24 to 36 hours. In 5 subjects no early fall in cardiac output was observed, but it fell 24 to 48 hours after administration. The character of the electrocardiographic records suggested that digitoxin increased the strength of myocardial contraction and slowed the rate of ventricular diastolic filling. The duration of the phases of the cardiac cycle, determined for the right and left ventricles, was unchanged. The heart rate was unaltered except in one subject who had a bradycardia on the fourth day after taking digitoxin.

The authors conclude that digitoxin decreases the venous return and increases the force of cardiac contraction.

D. Verel

**482. Effect of Intravenous Digitoxin on Fluid Distribution in Hospitalized Males without Cardiovascular Disease**

J. K. AIKAWA, V. H. KNIGHT, and M. P. TYOR. *Proceedings of the Society for Experimental Biology and Medicine [Proc. Soc. exp. Biol., N.Y.]* 76, 250-252, Feb., 1951. 3 refs.

The authors have determined the effect of intravenous digitoxin on plasma and extracellular-fluid volume in normal individuals. The serial studies were carried out on 5 male patients with non-cardiovascular disorders and with no obvious disturbances of salt and water metabolism.

Commercial crystalline digitoxin in 40% alcohol, 0.2 mg. per ml., was used and the haematocrit value, plasma volume, thiocyanate space (Aikawa, *Amer. J. Physiol.*, 1950, **162**, 695), and serum protein concentration (Kingsley, *J. Lab. clin. Med.*, 1942, **27**, 840) were determined. The serum protein concentration and the plasma volume were used in calculating the total circulating protein content. Base-line determinations being completed, digitoxin was injected intravenously in 2 equal doses of 0.6 mg., one hour apart. After 5 hours, venous blood was withdrawn and a solution containing Evans blue and sodium thiocyanate was injected. The plasma and total blood volumes were calculated from samples withdrawn 10 minutes later, and the thiocyanate space was calculated from a sample withdrawn 3 hours later (8 hours after initial digitoxin). The total serum protein was estimated on 5-, 7-, and 8-hour samples, and haematocrit values on 5- and 8-hour samples. All the tests were repeated after 72 hours.

The results showed a significant decrease in concentration of serum proteins and an increase in the mean total circulating protein content within 8 hours. This was associated with a suggestive increase in mean plasma volume and a decrease in haematocrit value, indicative of either a primary shift of water and a secondary mobilization of labile protein into a vascular compartment or a primary shift of protein-containing fluid into a vascular compartment.

Malcolm Woodbine

**483. Circulatory and Respiratory Effects of Adenosine Triphosphate in Man**

D. F. DAVIES, A. L. GROPPER, and H. A. SCHROEDER. *Circulation [Circulation]* 3, 543-550, April, 1951. 2 figs., 28 refs.

**484. Analysis of the Actions of Acetylcholine, Atropine, Epinephrine and Quinidine on Heart Muscle of the Cat**

J. R. DiPALMA and A. V. MASCATELLO. *Journal of Pharmacology and Experimental Therapeutics [J. Pharmacol.]* 101, 243-248, March, 1951. 2 figs., 11 refs.

The isolated auricle of the cat was suspended in 30 ml. of Locke's solution and oxygenated with 95% oxygen and 5% carbon dioxide. The temperature was maintained at 30°C. and stimulation was effected by dual square waves through silver electrodes coated with silver chloride. In each experiment the muscle was "warmed up" to maximal activity by stimulating at a rate of 75 per minute for 5 minutes. The first stimulus drove the muscle at a given rate and the second was used to measure the refractory period. The resting excitability was measured by determining the minimal amount of current in milliamperes which was capable of stimulating the muscle at durations of stimuli of 17, 10, 5, 2.5, 1.0, and 0.1 m.sec. respectively. The amplitude of contraction was measured from tracings made with an isometric lever. The doses of the drugs found to yield a satisfactory response were: acetylcholine 100 µg., atropine 250 µg., adrenaline 100 µg., and quinidine 1 mg.

The effect of acetylcholine on excitability was complex. It increased the rheobase, but shortened the chronaxie. Atropine restored the *status quo*. Given independently,

atropine decreased the resting excitability, adrenaline increased it, and quinidine decreased it. Acetylcholine shortened the refractory period, as did adrenaline in lesser degree. The refractory period was lengthened by atropine and by quinidine. Acetylcholine decreased contractility, but this was restored to normal by atropine. Atropine given alone had little effect. Adrenaline increased contractility of both the auricle and papillary muscle. Quinidine decreased the contractility of the auricle slightly, but had a greater effect on the papillary muscle.

Spontaneous activity of the muscle was always stopped by acetylcholine, and was always restored by the addition of atropine. Adrenaline started spontaneous activity if the muscle was quiescent, and increased the rate if activity was already present.

P. A. Nasmyth

**485. The Metabolism of the Heart in Relation to Drug Action. VI. Metabolic Actions of Quinidine on Rat Heart Muscle**

J. L. WEBB, P. R. SAUNDERS, and K. NAKAMURA. *Journal of Pharmacology and Experimental Therapeutics* [J. Pharmacol.] 101, 287-295, March, 1951. 5 figs., 11 refs.

The utilization of endogenous oxygen by slices of rat's ventricle and auricle was measured manometrically in air. In the absence of added substrate, oxygen utilization by both auricle and ventricle was depressed when, 40 minutes after the start of the experiment, quinidine was tipped into the vessels from the side-arm. The percentage inhibition for both auricle and ventricle was similar and increased with time up to 80 minutes, when the inhibition averaged 27% with a concentration of quinidine of  $3 \times 10^{-4}$  M.

The addition of pyruvate, lactate, succinate, or malate to slices of rat's ventricle 1½ hours after the start of the experiment increased the absolute oxygen uptake. The effect of quinidine on this phenomenon was slightly to increase it. Quinidine inhibited by about 15% the increased oxygen uptake caused by oxalacetate. The respiration of ventricle slices was depressed by quinidine in the absence of glucose, and to a lesser extent in its presence. This suggested that quinidine does not inhibit the increased oxygen uptake occasioned by glucose.

Anaerobic glycolysis was measured by the manometric determination of evolved  $\text{CO}_2$  and by the determination of lactic acid. Quinidine ( $3 \times 10^{-4}$  M) inhibited anaerobic glycolysis strongly, though the onset of inhibition did not occur so quickly as the depression of oxygen uptake. Ultimately (1½ hours after the addition of quinidine) the inhibition of glycolysis was greater than the depression of oxygen uptake. Quinidine ( $3 \times 10^{-4}$  M) inhibited by 14% the hydrolysis of adenosine triphosphate by rat-ventricle homogenates. In 20 minutes  $5 \times 10^{-5}$  M quinidine decreased the spontaneous rate of contraction of the isolated rat heart by 50%. The refractory period of isolated auricles was increased by  $1 \times 10^{-4}$  M quinidine, and to the same extent in one-third of the time by a  $3 \times 10^{-4}$  M concentration. The spontaneous rate was also reduced by these concentrations.

P. A. Nasmyth

**486. Quinidine Sulfate in Propylene Glycol by Intramuscular Injection in Man**

J. L. GLUCK, H. GOLD, T. GREINER, W. MODELL, N. T. KWIT, S. THICKMAN, H. L. OTTO, and J. L. WARSHAW. *Journal of the American Medical Association* [J. Amer. med. Ass.] 145, 637-640, March 3, 1951. 5 figs., 8 refs.

The frequency of gastro-intestinal symptoms following quinidine by mouth has prompted the search for a safe intramuscular preparation. Disadvantages encountered up to now have been instability and pain at the site of injection, but it is claimed that a 20% solution of quinidine sulphate in ethylene glycol will remain stable for 6 months and cause less local reaction on injection than penicillin. Its action on the heart was therefore tested in 7 patients with slow fibrillation of long duration and varied aetiology, using doses of 0.4 to 0.6 g. A total of 170 electrocardiograms were analysed: maximum slowing of the auricles averaged over 20% and occurred in 3 hours, 50% of the maximum being present at 1 hour and persisting up to 8 hours. Results were slightly greater with the higher doses and agreed well with those obtained by the oral route. A dosage scheme of 0.4 g. 6-hourly produced increasing effects for the first 4 to 6 injections, after which there was a persistent plateau of about 30% slowing. A patient with thyrotoxic flutter, who failed to respond to digitalis and in whom quinidine by mouth produced diarrhoea without altering the rate, reverted to normal rhythm after the eleventh dose of 0.4 g. quinidine given intramuscularly at 3-hourly intervals.

A. Paton

**487. Quinidine-induced Exfoliative Dermatitis. With a Brief Review of Quinidine Idiosyncrasies**

D. R. TAYLOR and R. POTASHNICK. *Journal of the American Medical Association* [J. Amer. med. Ass.] 145, 641-642, March 3, 1951. 11 refs.

Gastro-intestinal disturbances and cinchonism are well-known side effects of quinidine, and cardiac standstill, transient respiratory arrest, and anaphylactic shock may occur during administration: rare toxic effects such as thrombocytopenic purpura, eczematoid reactions, sinus thrombosis, and pyrexia have also been reported.

The authors describe the case of a man of 59 who was given 0.2 g. quinidine by mouth 4-hourly for attacks of supraventricular tachycardia of 25 years' duration. The attacks ceased, but nearly 3 weeks later, while still taking quinidine, he developed a pustular eruption which, however, responded to penicillin. A maculopapular rash appeared 18 days later which was thought to be due to penicillin and was treated with benadryl; this also subsided, only to be followed in a fortnight by extensive exfoliation, accompanied by enlargement of liver, spleen, and lymph nodes, jaundice, and considerable disturbance of liver function. At this stage quinidine was stopped and in 3 weeks the patient had returned to normal health. A further attack of tachycardia occurred and quinidine was again given, with almost immediate exfoliation. Once more the drug was stopped, and this time digitalis was substituted without ill effects.

A. Paton

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**488. Rutin and Other Flavonoids as Potentiators of Terminal Vascular Responses to Epinephrine and as Antagonists of Vasodepressor Materials**

J. M. CRIMSON, R. R. BEREZ, J. D. MADDEN, and F. A. FUHRMAN. *American Journal of Physiology* [Amer. J. Physiol.] **164**, 391-399, Feb., 1951. 1 fig., 30 refs.

The technique of Chambers and Zweifach for the study of the capillary bed in the mesoappendix of rats was used. Alterations in the threshold concentration of locally applied adrenaline necessary to produce constriction of metarterioles and precapillaries were observed as a measure of activity. Rutin dissolved in propylene glycol and given intravenously in doses of 2.5 to 50 mg. per kg., reduced the adrenaline threshold to about 40% of the control level. Oral administration was effective within 75 minutes for 5½ hours. Rutin antagonized the vascular effects of oedema fluid from frost-bitten limbs and of hepatic vasodepressor material (ferritin). Sodium rutin acid succinate, methylated hesperidin chalcone, and sodium hesperidin chalcone also reduced the adrenaline threshold.

*A. Schweitzer*

**489. The Nature of Uterine and Intestinal Sympathin**

M. MANN and G. B. WEST. *British Journal of Pharmacology and Chemotherapy* [Brit. J. Pharmacol.] **6**, 79-82, March, 1951. 10 refs.

Cats were anaesthetized with chloralose and received either heparin or chlorazol fast pink as anticoagulant. Uterine blood was collected from the left ovarian vein, and intestinal blood from the inferior mesenteric vein. Stimulation of the left hypogastric nerve below the inferior mesenteric ganglion was followed by the appearance of adrenaline and noradrenaline in the uterine blood, and stimulation of the inferior mesenteric nerve by their appearance in the intestinal blood. Assay was by the authors' method (Brit. J. Pharmacol., 1950, **5**, 173). Average concentrations in  $\mu\text{g.}$  per ml., were 0.037 of noradrenaline and 0.005 of adrenaline in the uterine blood, and 0.044 of noradrenaline and 0.013 of adrenaline in the intestinal blood, on stimulation of the appropriate nerves. Noradrenaline was absent in two uterine experiments out of 13. It was present in all the others.

*V. J. Woolley*

**490. Adrenalinogen, Adrenaline, and Sympathetic Stimulation. (Adrenalinogen, Adrenalin und Sympathicureiz)**

G. LEHMANN and H. KINZIUS. *Pflügers Archiv für die Gesamte Physiologie* [Pflüg. Arch., ges. Physiol.] **253**, 132-151. 10 figs., 41 refs.

Attention is drawn to the observation that fluorometric and chemical estimations of adrenaline in blood yield higher values than corresponding biological methods (Lehmann and Michaelis, *Arbeitsphysiologie*, 1942, **12**, 264). Since the "inactive adrenaline" appears to be a precursor of adrenaline, the authors propose that it be termed "adrenalinogen".

If a dog's heart is stimulated by warming the sino-auricular node or by electrical stimulation of the sympathetic, after a definite delay there is an arterio-

venous difference in adrenalinogen content of the coronary blood. Stimulation of the sympathetic innervation of a limb produces a similar result. In both cases the difference is caused rather by a rise in arterial blood content than by a fall in the venous blood. There is also a secretion of adrenalinogen from the adrenal medulla. By transfusing venous blood from the heart or limb of a dog subjected to such stimulation to the circulation of another, the release of medullary adrenalinogen in the second animal can be shown to be a humoral process. The injection of small quantities of adrenaline or noradrenaline also causes a release of adrenalinogen in the dog. An electrically induced convulsion produces a considerable secretion of adrenalinogen from the medulla. If a dog is given a convulsion and venous blood is transfused from it to a second dog, vigorous secretion of adrenalinogen begins more quickly in the second than in the first.

These results lead to the suggestion that adrenalinogen from the adrenal medulla reaches the sympathetic nerves, where it forms depots, via the circulation. Sympathetic stimulation converts the adrenalinogen to adrenaline, with progressive depletion of these peripheral depots. The liberated adrenaline causes a further secretion of adrenalinogen from the adrenal medulla, which is available for replenishing the depots' stores.

*Norval Taylor*

**491. Effect of Adrenaline on Resistance to Gas Flow in the Respiratory Tract and on the Vital Capacity of Normal and Asthmatic Subjects**

M. B. SHELDON and A. B. OTIS. *Journal of Applied Physiology* [J. appl. Physiol.] **3**, 513-518, March, 1951. 4 figs., 11 refs.

In 6 healthy and 6 asthmatic subjects the authors measured vital capacity and resistance to gas flow, the latter by measuring alveolar pressures by a method previously described (Otis and Proctor, *Amer. J. Physiol.*, 1948, **152**, 406; Otis and Bembower, *J. appl. Physiol.*, 1949, **2**, 300). In the normal group no significant changes occurred in the vital capacity following the subcutaneous injection of from 0.35 to 0.5 ml. of 1 in 1,000 adrenaline hydrochloride. Three of these subjects showed a moderate decrease in resistance to gas flow after adrenaline. All asthmatic subjects showed an increase in vital capacity after adrenaline. In 4 the resistance to flow decreased, in 1 it remained unchanged, and in 1 it rose.

The authors suggest, in view of this finding, that adrenaline may increase vital capacity in 2 different ways: (1) by dilating the bronchioles, which would also lower the resistance to air flow; (2) by constricting pulmonary blood vessels, which would have little or no effect on the resistance to air flow. Either or both of these types of action may occur in any individual. It is further suggested that the different effects of adrenaline may correspond to different aetiological factors giving rise to the same symptomatology, and that the response to adrenaline may be useful in determining the underlying cause in any given case of "asthma".

*P. Mestitz*

492. "Tifen", an Antispasmodic Drug. (Спазмолитическое средство тифен)

M. D. MASHKOVSKI and S. S. LIBERMAN. Советская Медицина [Sovetsk. Med.] No. 1, 31-32, 1951.

"Tifen", an antispasmodic drug, was synthesized at the Ordzhonikidze Institute. It is the hydrochloride of the diethylaminoethyl ester of thiadiphenylacetic acid, and is a white, crystalline powder of bitter taste. Its action resembles, but is 3 to 4 times stronger than, that of papaverine; it has some atropine-like properties, as it acts as an antagonist to acetylcholine and carbachol. When carbachol, 0.001 mg. per kg. body weight, was given intravenously to cats, the tone and peristalsis of the intestines were greatly increased. Tifen, 3 to 5 mg. per kg. body weight, relaxed the spasm completely. Strong antispasmodic activity of the drug was noted on the smooth muscle of the blood vessels. When tifen, 1 : 200,000, was passed through the isolated heart of a rabbit, the flow of the fluid increased by about 50 to 60%. When the same experiment was performed with papaverine the flow increased only 25 to 30%. [This experiment was carried out according to the technique of Kravkov and Pisemski, no details of which are given.]

Tifen has a slight analgesic effect. A solution containing 0.5% of the drug was injected into the conjunctiva of rabbits and produced a reduction of its sensitivity; a 1.0% solution led to a strong inflammatory reaction. The drug proved to be of very low toxicity and did not have any appreciable effect on respiration or cardiac action. Tifen, in a dose of 0.55g. per kg. body weight subcutaneously or 15 mg. per kg. intravenously, produced a 50% mortality rate in white mice. Papaverine, 0.3 g. per kg. subcutaneously or 10 mg. per kg. intravenously, produced the same result.

The drug was tried clinically for various complaints. Patients who received it all suffered from "some form of spastic disease of the blood vessels" (migraine, angina, gastric ulcer, bronchial asthma). The dose was 0.03 g. thrice daily by mouth or 1.0 ml. of a 0.5% solution subcutaneously for about 35 days. No side-effects were reported and spastic symptoms were thought to be relieved by the drug. Tifen has now been released for general use.

N. Chatelain

493. Unmasking, after Cholinergic Paralysis by Botulinum Toxin, of a Reversed Action of Nicotine on the Mammalian Intestine, Revealing the Probable Presence of Local Inhibitory Ganglion Cells in the Enteric Plexus  
N. AMBACHE. *British Journal of Pharmacology and Chemotherapy* [Brit. J. Pharmacol.] 6, 51-67, March, 1951. 12 figs., 18 refs.

It is known that the toxin of *Clostridium botulinum* has a selective affinity for cholinergic nerve endings and thus paralyses motor neurones. By using isolated mammalian intestinal preparations the effect of the toxin on the peristaltic reflex has been studied. Mice were first injected subcutaneously or intraperitoneally with dilutions of the culture-broth, and just after death (due to systemic botulism) a portion of the ileum was removed and examined for peristaltic activity. A liquid bolus of Tyrode's solution was entrapped in the piece of

gut, which was ligated at both ends. This distending stimulus produced peristalsis in normal preparations, but in mice showing severe generalized locomotor paralysis before death peristalsis was absent and the normal response to nicotine was almost abolished. The cholinergic nerve plexus had been blocked in these injected animals.

In rabbits under ether anaesthesia, local injections of toxin were given into the intestinal wall between the longitudinal muscle layer and its peritoneal covering. The dose was divided into two parts and given at two points about 5 to 10 cm. apart. After recovery from the anaesthetic the animal died in 3 to 7 hours, when the piece of jejunum or ileum between the two injection points was excised. In this way, a small portion of the gut contained a high concentration of toxin. This piece was set up in an isolated-organ bath in Tyrode's solution without magnesium. In 15 botulinized preparations there was a loss of the normal intestino-motor action of nicotine. In some cases a reversal of the motor action was seen immediately, while in others it occurred soon after setting up the preparation. Even when the motor response to nicotine was lost the otherwise normal behaviour of the intestine was indicated by the presence of pendular movements and of strong motor responses to acetylcholine and to eserine.

The inhibitory action of nicotine on the botulinized gut was shown to be due to stimulation of nerve cells in the wall of the intestine, for it did not occur when these cells were paralysed either by large doses of nicotine or by hexamethonium (2 mg.). The inhibitory action of small doses of nicotine in the poisoned intestine resembled an adrenaline effect and was abolished by high concentrations of ephedrine. It is suggested, therefore, that ganglia are activated by the nicotine which are the cell bodies of short adrenergic neurones. Two kinds of functionally distinct ganglion cells are probably present in the myenteric plexus.

G. B. West

494. The Anticoagulant Properties of Sulphonated Proteins. (Über sulfurierte Proteine und ihre Eigenschaften als Blutantikoagulantien)

H. C. REITZ and H. CORDS. *Biochemische Zeitschrift* [Biochem. Z.] 321, 414-420, March 21, 1951. 11 refs.

Various proteins of human, bovine, and vegetable origin were sulphonated by means of pyridine and chlorosulphonic acid at different temperatures. The anticoagulant power of the water-soluble derivatives was about 5 to 10% of that of heparin. The amount of sulphur entering the protein molecule varied directly with the temperature of sulphonation and ranged from 3 to 8%. The solubility in water of the sulphonated protein was unrelated to its sulphur content or to the solubility of the parent protein. For the different sulphonated derivatives of any one protein, the anticoagulant power was directly proportional to the sulphur content, but the anticoagulant powers were different for different proteins having the same sulphur content. The anticoagulant power of phosphorylated egg albumin containing 3.7% phosphorus was 6.5% compared with heparin.

The toxicity of the sulphonated proteins was determined in rats by injecting intravenously quantities of a 7% solution in phosphate buffer at pH 7.6 ranging from 14 to 349 mg. per kg. of body weight. In general, the toxicity was too high for the substances to be of practical value as anticoagulants.

M. Lubran

### CHEMOTHERAPY

#### 495. Serum Concentrations of *para*-Aminosalicylic Acid (PAS) Produced by Various Forms of PAS

D. K. DUNCAN, D. T. CARR, K. H. PFUETZE, and M. H. POWER. *Diseases of the Chest [Dis. Chest]* **19**, 138-144, Feb., 1951. 7 refs.

The serum concentration of free and total *para*-aminosalicylic acid (PAS) in 26 patients was determined after single and repeated oral doses of the free acid in powder form and of the sodium salt. Approximately the same concentrations were given by both the acid and the sodium salt, the mean figures 1½ hours after a single dose being  $5.6 \pm 0.35$  and  $6.9 \pm 0.41$  mg. per 100 ml. for the free acid and sodium salt respectively. Compressed tablets or enteric-coated granules gave lower concentrations, possibly due to delayed absorption. The sodium salt was better tolerated, causing less gastro-intestinal irritation.

R. Wien

#### 496. The Adsorption of Digestive Enzymes by Sulphonamides

G. CRONHEIM and J. S. KING. *Journal of Pharmacology and Experimental Therapeutics [J. Pharmacol.]* **101**, 230-236, Feb., 1951. 1 fig., 5 refs.

Sulphonamides have previously been shown to prevent the inactivation of penicillin by penicillinase due to the physical adsorption of the enzyme on the sulphonamide particles. The effect of a number of sulphonamides, in both macro- and microcrystalline forms, on the activity of pepsin, trypsin, pancreatin, and malt diastase was studied. The technique used was to add various amounts of the sulphonamide to 10 ml. of the enzyme solution. The suspension was shaken occasionally, centrifuged after 15 minutes, and the enzyme activity remaining in the clear supernatant fluid then measured.

The results showed that all the enzymes were adsorbed by each of the 15 different sulphonamides investigated. The degree of adsorption depended on the amount of the sulphonamide present and its particle size. Sulphadiazine adsorbed the greatest amount of enzyme, followed by maphenide (marfanil), sulphamerazine, sulphathiazole, and sulphadimethylpyrimidine. Sulphaguanidine and sulphanilamide adsorbed the smallest amount of enzyme. The order of adsorptive capacity seems to be related qualitatively to the pKa values of the different sulphonamides. The adsorption of pepsin on microcrystalline sulphathiazole apparently causes some irreversible change, because only part of the enzyme activity could be found following separation from the sulphonamide.

R. Hodgkinson

### ANTIBIOTICS

#### 497. Terramycin: Clinical, Pharmacologic, and Bacteriologic Studies.

R. J. SAYER, J. C. MICHEL, F. C. MOLL, and W. M. M. KIRBY. *American Journal of the Medical Sciences [Amer. J. med. Sci.]* **221**, 256-263, March, 1951. 2 figs., 2 refs.

Terramycin was used in the treatment of 108 cases of infection due to Gram-positive and Gram-negative organisms. Preliminary sensitivity tests *in vitro* had shown that the organisms concerned were highly sensitive, with the exception of 14 strains of *Bacterium coli* which grew in 50 µg. terramycin per ml. Adults receiving 1 g. orally 6-hourly maintained blood levels of 5 to 10 µg. per ml. throughout the day. Children were given doses in proportion to weight. Intravenous administration of 250 mg. gave a blood level of 5 to 10 µg. per ml. 1 hour later and 1 to 5 µg. after 12 hours. Toxic reactions, such as nausea, vomiting, and loose stools, were uncommon. Clinical improvement was seen in 24 of the 28 patients with urinary infection, in 18 of 21 children with pertussis, and in 22 of 25 children and all 13 adults with pneumonia. Favourable responses occurred in bacillary dysentery, tonsillitis, erysipelas, bronchiectasis, and typhoid fever.

I. Ansell

#### 498. Side-effects of Chloramphenicol and Aureomycin, with Special Reference to Oral Lesions

T. TOMASZEWSKI. *British Medical Journal [Brit. med. J.]* **1**, 388-392, Feb. 24, 1951. 4 figs., 26 refs.

The author, working at the Royal Infirmary, Edinburgh, describes the side-effects observed in 70 patients receiving 2 g. daily of chloramphenicol (average total 32 g.) and 56 patients receiving 2 g. daily of aureomycin (average total 28 g.). General reactions, such as drowsiness, malaise, or skin rashes, were rare. Oral manifestations occurred in over 50% of cases, were commonest in young women, and developed more rapidly in cases previously treated with penicillin and streptomycin. An atrophic glossitis was frequently seen; hypertrophic glossitis with brown discolouration of the tongue was less common. Scrapings from the tongue revealed the replacement of the usual bacterial flora by fungi, usually *Candida albicans*. Dryness of the mouth with sore throat, interference with taste, redness of the mouth with blisters, and angular stomatitis similar in appearance to vitamin-B deficiency were also seen and responded to vitamin-B-complex therapy. Gastro-intestinal symptoms, such as flatulence, nausea, and diarrhoea, were commoner with aureomycin, as also were rectal and genital changes.

I. Ansell

#### 499. Absorption and Excretion of Viomycin in Humans

C. A. WERNER, C. ADAMS, and R. DUBois. *Proceedings of the Society for Experimental Biology and Medicine [Proc. Soc. exp. Biol., N.Y.]* **76**, 292-295, Feb., 1951. 1 fig., 6 refs.

This study of viomycin, another product of a *Streptomyces* which is of interest in the treatment of tuberculous infections, comes from the Department of Medicine of the New York Hospital, Cornell Medical Center.

The antibiotic was supplied in 1-g. vials as the purified sulphate and dissolved in sterile distilled water (250 to 500 mg. per ml.) for intramuscular injection. The microbiological assay of viomycin in serum, urine, and cerebrospinal fluid was performed by a modified tube-dilution method using *Klebsiella pneumoniae*, Type A-D, as the test organism. All concentrations were expressed in terms of pure viomycin base having a potency of 1,000 µg. per mg.

Single intramuscular doses of 25 to 50 mg. per kg. were given to each of 5 adult males. The highest serum concentration was reached in  $\frac{1}{2}$  to 2 hours and ranged from 82 to 125 µg. per ml. No viomycin was detectable after 24 hours. The smallest concentration detectable by this method was 7.5 µg. per ml. Urinary excretion commenced within an hour of injection and concentrations up to 12 mg. per ml. were reached. Some 65 to 100% of the administered dose was recovered within 24 hours. The concentrations in 22 sera, obtained during maintenance therapy in 6 patients with pulmonary tuberculosis receiving 1 g. intramuscularly twice or thrice daily, were determined. In 8 out of 14 no antibiotic was detectable 12 hours after the last dose, but in the 6 remaining specimens concentrations of 7.5 to 30 µg. per ml. were present. In the other 8 specimens concentrations of 30 to 100 µg. per ml. were present 4 hours after injection. In 3 specimens of cerebrospinal fluid concentrations of 4 to 12.5 µg. per ml. corresponded to serum concentrations of 100 to 125 µg. per ml. There was no evidence of any meningeal involvement.

Malcolm Woodbine

**500. Viomycin in Tuberculosis of Guinea Pigs due to Streptomycin - sensitive and to Streptomycin - resistant Tubercle Bacilli**

A. G. KARLSON and J. H. GAINER. *Proceedings of the Staff Meetings of the Mayo Clinic* [Proc. Mayo Clin.] 26, 53-59, Jan. 31, 1951. 3 figs., 12 refs.

The authors briefly refer to previous papers on viomycin, and describe two experiments in which guinea-pigs were employed. In the first experiment 36 guinea-pigs of 850 g. weight were infected with a streptomycin-sensitive strain of tubercle bacillus of human type (H37 Rv), and in the second experiment 36 similar animals were infected with a streptomycin-resistant strain of the same organism; 24 days later six guinea-pigs from each experiment were killed as pre-treatment controls. In each experiment 10 animals were treated with 6 mg. of streptomycin once daily, and 10 were given 20 mg. of viomycin once daily. The remaining animals acted as controls. Treatment continued from the 24th to the 61st day, when all the animals were killed.

In the first experiment all the controls had extensive tuberculosis, whereas only minimal lesions were found in those treated with streptomycin or viomycin. In the second experiment the viomycin-treated animals were found to have developed minimal lesions, whereas both the controls and the streptomycin-treated group showed widespread tuberculosis.

The animals given viomycin continued to gain weight during the entire treatment period. No morphological

changes that could be attributed to toxic effects of viomycin were seen on microscopical examination of lung, liver, spleen, or kidney.

A. W. H. Foxell

**501. Fumagillin (H-3), a New Antibiotic with Amebicidal Properties**

M. C. McCOWEN, M. E. CALLENDER, and J. F. LAWLIS. *Science* [Science] 113, 202-203, Feb. 23, 1951. 4 refs.

An antibiotic has been isolated from a species of *Aspergillus* which has little antibacterial or antifungal activity and no action on the viruses tested. However, it does have a very marked effect *in vitro* on the growth of *Entamoeba histolytica*. When a mixed bacterial flora was present the minimal effective concentration varied from 1 in 8,192,000 to 1 in 131,072,000. In the absence of bacteria the minimum inhibitory concentration was 1 in 4,096,000. Since no associated bacterial growth influenced the growth of the amoebae the action of fumagillin is apparently directly on the amoeba. In young rats and rabbits infected with *E. histolytica* excellent therapeutic results were obtained. In rats the total dosage was 36 mg. per kg. in 2 days, and in rabbits 100 mg. per kg. in 2 days. The antibiotic was ineffective *in vivo* against *Spirochaeta novyi* and *Trypanosoma gambiense* or *T. equiperdum* in mice.

G. M. Findlay

**502. Monilial Infections Complicating the Therapeutic Use of Antibiotics**

J. W. WOODS, I. H. MANNING, and C. N. PATTERSON. *Journal of the American Medical Association* [J. Amer. Med. Ass.] 145, 207-211, Jan. 27, 1951. 2 figs., 2 refs.

By the suppression of bacterial growth the administration of antibiotics may have an enhancing effect on the growth of fungi. The authors describe 25 cases of moniliasis occurring apparently as a direct sequel to antibiotic therapy, in which the presence of *Candida* (*Monilia*) *albicans* was confirmed in all cases by culture. The cases fall into three groups.

Group 1. Regardless of the route of administration, penicillin, aureomycin, and chloramphenicol might lead to oropharyngeal and oesophageal moniliasis. It usually appeared 24 to 72 hours after the condition which was the reason for antibiotic therapy had disappeared, but might occur during antibiotic treatment. The tongue, buccal mucosa, sense of taste, and/or any part of the upper alimentary tract might be affected. Four cases are reported in detail and 16 cases are tabulated under the headings of age, antecedent antibiotic treatment, and clinical symptoms. The tongue was affected in all cases.

Group 2. Infection of the intestinal tract, with diarrhoea. The presenting complaint was usually that of a mild persistent diarrhoea which developed after antibiotic treatment of some infection usually not related to the gastro-intestinal tract. Culture of faeces on Sabouraud's medium revealed *C. albicans* in significant numbers. No other potentially pathogenic organisms were present to account for the illness. Of 3 cases described in detail, in 2 there was also generalized urticaria as a result of penicillin sensitivity. An additional 3 cases are mentioned in which *C. albicans* was

isolated as the predominant organism on stool culture without giving rise to intestinal symptoms.

Group 3. Two cases are described in which bronchopulmonary moniliasis appeared as a complication of antibiotic treatment for acute and chronic pulmonary infections. In both cases skin tests and agglutination tests for *Candida* were positive; desensitization with increasing strength of monilial vaccine was carried out.

The factors possibly responsible for the occurrence of the monilial infection are discussed. The most likely cause appears to be the suppression of the bacterial flora competing with *Candida* for nutrition in the same substrate.

Ferdinand Hillman

**503. Clinical and Biologic Significance of Penicillin-resistant Staphylococci, including Observations with Streptomycin, Aureomycin, Chloramphenicol, and Terramycin**

W. W. SPINK. *Journal of Laboratory and Clinical Medicine* [J. Lab. clin. Med.] 37, 278-293, Feb., 1951. Bibliography.

This well documented paper on the incidence of penicillin-resistant, coagulase-positive staphylococci comes from the Department of Medicine, Minnesota University Hospitals and Medical School. The 104 strains isolated were also examined *in vitro* with streptomycin hydrochloride, chloramphenicol, aureomycin, and terramycin hydrochloride.

The sensitivity of the organisms was assessed by two-fold dilutions in tubes (0.0078 to 4,000  $\mu\text{g}$ . per ml.; chloramphenicol was tested at 250  $\mu\text{g}$ . per ml., its maximum solubility) with inocula of 0.5 to  $1 \times 10^6$  organisms. Of the 104 strains 46 were inhibited by 0.5 unit or less of penicillin per ml. and were called sensitive, and 45 (43.2%) were resistant to 62.5 units or more of penicillin per ml. and were considered highly resistant: 25 of these last (24% of the total) needed more than 500, 4 needed 2,000, and 2 over 4,000 units per ml. The penicillinase produced by all the resistant strains from human cases inhibited the high concentration of 1,000 units per ml., and no penicillinase was found in sensitive cells.

Only 2 strains were resistant to penicillin and streptomycin (1 being resistant to neomycin also). Similar results were obtained with streptomycin or dihydrostreptomycin, and 20 strains were resistant to over 62.5  $\mu\text{g}$ . per ml. Every strain resistant to streptomycin was also very resistant to penicillin, and 9 strains grew in the presence of over 4,000  $\mu\text{g}$ . per ml. All streptomycin-resistant strains were sensitive to chloramphenicol and aureomycin, and all except 2 to terramycin. With one exception all staphylococci were sensitive to therapeutic concentrations of aureomycin, and although no patients had received terramycin, 5 strains were resistant to terramycin and no strain was resistant to aureomycin and sensitive to terramycin. Weight for weight, all staphylococci were more resistant to chloramphenicol than to either aureomycin or terramycin; 4 strains were resistant to penicillin and chloramphenicol.

The author emphasizes that penicillin-sensitivity determinations should also include "due consideration . . . to the optimum activity of penicillinase" for

example, by the use of large inocula of 0.5 to  $1.0 \times 10^6$  organisms. Although it is possible to produce anti-penicillinase sera, it is much better to administer an antibiotic unaffected by penicillinase. If sensitivity tests with penicillin, streptomycin, aureomycin, chloramphenicol, and terramycin cannot immediately be carried out, treatment of staphylococcal infections with aureomycin will minimize the problem of resistance to antibiotic therapy.

Malcolm Woodbine

**504. Penicillin Intolerance as a Sensitization Problem. (Die Penicillin-unverträglichkeit als Sensibilisierungsproblem)**

E. H. GRAUL and R. MENZEL. *Hautarzt* [Hautarzt] 2, 55-62, Feb., 1951. Bibliography.

After a review of the literature the authors describe 2 cases of severe reaction after administration of penicillin. The number of reactions, some due to pure penicillin, others to impurities and to the various vehicles, has been on the increase since 1948. Several deaths have been reported. Some patients recover from a severe reaction and tolerate further penicillin without mishap. The generally accepted opinion that mycotic infection predisposes to penicillin sensitivity is again confirmed. The active principle in pure penicillin allergy is not known, but it is suggested that the thiazolidine ring may be responsible. A similar ring is present in sulphathiazole. It is also thought that the side-chains of the penicillin molecule might link it with body proteins, thus producing the complete antigen.

G. W. Csonka

**505. Absorption and Clinical Use of Penicillin Preparations Given in Large Oral Doses. A Cooperative Study Utilizing Discontinuous Therapy**

P. BUNN, E. R. CALDWELL, C. ADAIR, M. LEPPER, and H. DOWLING. *Journal of the American Medical Association* [J. Amer. med. Ass.] 144, 1540-1543, Dec. 30, 1950. 1 fig., 9 refs.

The authors, working at the State University of New York and the George Washington University, Washington, present evidence to show that 500,000 units of various penicillin preparations, given by mouth, yields a moderate peak blood concentration, followed by an active lower, but consistent, level for 5 to 8 hours. This large dose was given 2 to 3 times a day, without a great increase in cost to the patient: it eliminated difficulties in arranging meals and assured the patient a good night's rest.

The several penicillin preparations are listed and included crystalline benzyl penicillin in orange syrup (10 patients); procaine penicillin tablets (8); benzyl penicillin tablets (67); benzyl penicillin in tap water (10); penicillin "O" (allylmercaptomethyl penicillin) in tap water (8); tablets of penicillin with aluminum (4); and benzyl penicillin in cherry syrup. These various preparations were administered to a total of 109 patients with pneumococcal,  $\beta$ -streptococcal, and miscellaneous infections. The response was satisfactory in 90% of the cases (including 26 out of 30 with lobar pneumonia, 5 out of 7 with bronchopneumonia, 16 out of 18 with scarlet fever, and 12 out of 13 with septic sore throat).

The serum concentration was determined in 40 cases after a dose of 200,000 to 500,000 units. With the latter dose the average serum level after 40 minutes was 0.8 unit per ml., with an average peak level after 1 hour of 1.7 unit per ml. The average level after 3 hours was 0.19 unit per ml., after 5 hours 0.09 unit per ml., and after 8 hours was 0.034 unit per ml. (49% with over 0.03 unit per ml.). Toxic reactions developed in only 2 patients. All the patients had a normally functioning gastro-intestinal tract before oral treatment started.

The authors conclude that oral administration in the majority of cases of infections by micro-organisms susceptible to penicillin is safe, easy, and reasonably inexpensive.

Malcolm Woodbine

#### 506. Penicillin Levels in Spinal Fluid after Intramuscular Injection of Procaine Penicillin

R. D. WRIGHT, J. D. THAYER, F. P. NICHOLSON, and R. C. ARNOLD. *Journal of Venereal Disease Information [J. vener. Dis. Inform.]* 32, 39-42, Feb., 1951. 6 refs.

Penicillin levels in the cerebrospinal fluid were determined on 198 specimens taken from 114 patients, 70 of whom had normal spinal fluids. Estimations were made at various intervals after a course of 600,000 units of procaine penicillin with 2% aluminium monostearate given every 24 hours for 6 doses. Serum levels as high as 0.6 unit per ml. were demonstrated after the last injection. Detectable levels of penicillin were obtained from 2 to 290 hours after the beginning of the injections, 82% of the specimens showing a level at 31 hours, and 91% at 122 hours.

From 22 patients given single injections of only 300,000 units, 4 of the specimens showed a measurable amount of penicillin in the cerebrospinal fluid and 8 showed a trace.

R. R. Willcox

#### 507. The Effect of Benemid on Plasma Penicillin Levels

J. F. WALDO and J. T. TYSON. *Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.]* 37, 272-277, Feb., 1951. 4 figs., 12 refs.

As 80% of penicillin is excreted through the renal tubules, the authors, working in the Department of Medicine of the University of Utah, have examined the effect of "benemid" (*p*-(*di-n*-propylsulphamyl)-benzoic acid) in suppressing this tubular excretion. Benemid was rapidly absorbed from the bowel, was free from systemic or renal toxicity, and enhanced the plasma penicillin levels in experimental animals.

In all, 15 subjects under 45 years of age, without renal disease, were given aqueous crystalline benzyl penicillin intramuscularly in doses of 200,000 units 8-hourly. Benemid was given orally in varying doses at varying time intervals, and penicillin levels determined 1, 3, 5, and 7 hours after administration of benemid.

Of 4 patients given 1 g. and one given 1.5 g. benemid one hour before the penicillin, all but one showed some elevation. Of 6 patients given multiple doses of 0.5 g. benemid 6-hourly (3 doses before estimation of the penicillin level), in 5 there was an appreciable elevation of the plasma penicillin level. There was also a cumu-

lative effect with benemid over 2 days, indicative of slow excretion. A patient with subacute bacterial endocarditis took 2 g. benemid a day with 2,000,000 units penicillin 8-hourly. This gave a more sustained level without any signs of toxicity over a period of 35 days.

The authors conclude that benemid seems to be a useful and effective agent for enhancing the plasma penicillin level.

Malcolm Woodbine

#### 508. Diffuse Encephalopathy after Streptomycin Treatment

J. R. EDGE. *Tubercle [Tubercle, Lond.]* 32, 58-60, March, 1951. 6 refs.

A man aged 44 was treated with 15 g. of *p*-aminosalicylic acid (PAS) and 1 g. streptomycin daily for 42 days. After 3 weeks he noticed transient mistiness of vision and deafness, and after 5 weeks he developed dizziness, which made it difficult to stand, and a generalized irritating rash. Three days after the end of treatment he was found collapsed on the floor. He was awake but unable to speak, to obey commands, or to recognize anyone; he was doubly incontinent. There were physical signs indicating a widespread cerebral lesion. Specimens of cerebrospinal fluid obtained on 4 occasions over a period of a month were normal. A streptomycin patch test gave an erythematous reaction. He was afebrile and had a regular pulse throughout. His condition at first deepened into stupor, but after 4 days progressive improvement started. After 2 months full speech and intellect were regained, but he could not see to read and had a spastic paralysis of the right arm and leg. Although there is no proof that streptomycin was the cause of his symptoms, the sequence of events is very suggestive.

L. M. Franklin

#### 509. Effect of Streptomycin on Vestibular Function

J. R. BIGNALL, J. W. CROFTON, and J. A. B. THOMAS. *British Medical Journal [Brit. med. J.]* 1, 554-559, March 17, 1951. 27 refs.

The effects of streptomycin on vestibular function were studied in 76 patients under treatment for pulmonary tuberculosis at the Brompton Hospital; 33 received 2 g. daily, 32 received 1 g. daily, and 11 patients received *p*-aminosalicylic acid (PAS) in addition to 1 g. daily of streptomycin. Observations on vestibular dysfunction included a record of symptoms of giddiness and nystagmus, leucocyte (eosinophil) counts, and caloric and galvanic tests. Caloric tests (response to stimulation of hot water into the ear) were performed at 44°, 30°, and 21° C.; galvanic tests were performed by placing one electrode over the mastoid region, when on gradually increasing the current to 4 to 8 mA the sensitivity of the nervous structures was indicated by a lateral inclination of the head towards the anode or away from the cathode.

Patients receiving 2 g. daily of streptomycin complained of giddiness much more than those receiving only 1 g. daily, the incidence in the latter group being 16%. Nystagmus on lateral deviation of the eyes was noted in 63% of patients receiving 2 g. daily, but in only 16% of those receiving 1 g. daily. There was a correlation between the caloric tests and symptoms of giddiness

and nystagmus, but the galvanic tests were positive in 13 patients who did not respond to the caloric tests. There was no relationship between the development of eosinophilia and the onset of giddiness. After prophylactic treatment with antihistamine drugs, the incidence of giddiness seemed to be reduced, suggesting that the antihistamine drugs may possibly be of some value in protecting against vestibular damage by streptomycin.

R. Wien

## TOXICOLOGY

### 510. Positive and Alternating Positive-Negative Pressure. Resuscitation from Curare Poisoning

S. W. HANDFORD and N. V. RICCHIUTI. *Journal of Applied Physiology* [J. appl. Physiol.] 3, 535-553, March, 1951. 4 figs., 35 refs.

Healthy dogs were used in these experiments. Apnoea was induced by the intravenous injection of D-tubocurarine. Various standard "resuscitators" were used to provide rhythmic insufflation of the lungs through a standard face mask. Provided that ventilation was begun before the onset of heart failure (as evidenced in this series by increasing amplitude of the T wave in the electrocardiogram) the 2 types of resuscitator (those providing intermittent positive and those providing alternating positive and negative pressures) gave equally satisfactory results, both during the acute stage of the experiments and as judged by the post-operative recovery of the animals. There is a detailed discussion of some of the finer points of various resuscitators at present in use in the U.S.A.

P. Mestitz

### 511. Lead-poisoning in Children. Report of Five Cases, with Special Reference to Pica

N. F. E. BURROWS, J. RENDLE-SHORT, and D. HANNA. *British Medical Journal* [Brit. med. J.] 1, 329-334, Feb. 17, 1951. 3 figs., 30 refs.

The authors describe 5 cases of lead poisoning in children seen in the Hospital for Sick Children, Great Ormond Street, London. They review the literature of the condition, now rare in Britain but not uncommon in Australia, U.S.A., and Japan. The infant may ingest lead from a dusting powder, a lead nipple shield, or the water supply; young children with perverted appetite (pica) may obtain lead from biting or sucking paintwork or leaden toys. The burning of battery cases as fuel has been the source of poisoning in older children.

Of the 5 cases 3 have occurred since 1948; histories of the other 2 were found in the hospital records. The children were aged respectively 7 years, 2½ years, 1 year 7 months, 5½ months, and 5 years. There was a history of debility with attacks of vomiting, abdominal pain, constipation, and anorexia. Four of the children suffered from pica; in one case the mother had used a lead nipple shield for 10 weeks. Anaemia, wasting, and hypotonia were found in all the children. Wrist-drop and a blue line along the gums were absent, but there was a marked tendency to the development of encephalopathy (shown by meningism, twitchings, coma, and convulsions) in 3 cases, and this was apparently precipitated

by lumbar puncture in 2. The blood in every case showed a hypochromic anaemia with punctate basophilia, recognized as significant; the lead content of the blood was above the normal in 2 cases. Glycosuria was present in 2 cases and excess of lead in the urine in 2. Radiography revealed typical dense lines of deposited lead at the growing ends of long bones and edges of flat bones. General treatment included a high calcium diet with milk and vitamin D, and doses of alkalis to encourage deposition of lead which, unless mobilized, remains innocuous.

Encephalopathy was treated by administration of magnesium sulphate by mouth and intramuscularly (25% solution) and 50% glucose intravenously. Convulsions and severe vomiting were controlled by intravenous injection of calcium gluconate, 10 ml. of a 10% solution. Two of the patients recovered clinically, but were mentally retarded; only one recovered completely. One child (aged 1 year and 7 months) died from perforated oesophageal ulcer, necropsy revealing evidence of lead poisoning. The ultimate history of the fifth child is not known. Prognosis is considered grave.

V. Reade

### 512. A Study of the Effect of Lipotropic Substances on the Liver in Dogs Poisoned with Carbon Tetrachloride. (Versuche über die Wirkung lipotroper Substanzen bei der durch Tetrachlorkohlenstoffvergiftung erzeugten Fettleber des Hundes)

F. HARTMANN and F. LEUSCHNER. *Archiv für experimentelle Pathologie und Pharmakologie* [Arch. exp. Path. Pharmak.] 212, 167-176, 1951. 3 figs., 41 refs.

Fatty changes were produced in the liver in 28 dogs by the oral administration of carbon tetrachloride. These changes were associated with a fall in the plasma phosphatide, lecithin, and sphingomyelin content. On cessation of treatment the fatty changes disappeared and the plasma phosphatide level rose. The lipotropic substances choline and methionine did not prevent the fatty changes occurring, but they accelerated the removal of neutral fat from the liver and the rise in plasma phosphatide level on the withdrawal of carbon tetrachloride.

R. Wien

### 513. Histological Investigations in Experimental Animals into the Effect of Dicumarol and Tromexan in High Dosage on the Liver and other Organs. (Histologische Untersuchungen an Versuchstieren über die Wirkung hoher Dicumarol- und Tromexan-dosen auf die Leber und andere Organe)

O. HUECK. *Archiv für experimentelle Pathologie und Pharmakologie* [Arch. exp. Path. Pharmak.] 212, 302-310, 1951. 31 refs.

A histological examination of the tissues in rats and rabbits after high doses of the anticoagulants dicumarol and tromexan showed very little change in any of the tissues examined except the liver. The pathological changes in the liver were mainly slight, but in some instances they were extensive, including central necrosis with nuclear changes and dilatation of the capillaries.

R. Wien

## Radiology

### 514. The Effect of Over-all Time of Exposure upon Survival of Young Chicks following Roentgen Irradiation

S. P. STEARNER and E. J. B. CHRISTIAN. *American Journal of Roentgenology and Radium Therapy* [Amer. J. Roentgenol.] 65, 272-276, Feb., 1951. 2 figs., 4 refs.

Unsexed White Leghorn chicks have been used 2 to 4 days after hatching to determine the relative influence of dosage rate and over-all time of whole body irradiation. A total dose of 1,000 r was given at rates of 6 r, 11.5 r, 18.5 r, and 43 r per minute in single exposures. The same dose was also given in 2 and 4 fractions at a dosage rate of 43 r per minute.

It was found that exposure to 1000 r given in two fractions was less lethal than when four fractions were given over the same period of time, so that a shorter time elapsed between doses; the latter was, however, less lethal than a continuous exposure for the same period of time at a lower dose rate. The authors suggest that recovery may increase with time after exposure. Increase in over-all time increased the survival of the chicks, but the proportion was not linear. The authors conclude that over-all time is more important than dose rate in determining the survival of chicks.

L. V. Pearce

### 515. The Theory and Methods of the Radioautographic Localization of Radio-elements in Tissues

J. GROSS, R. BOGOROCH, N. J. NADLER, and C. P. LEBLOND. *American Journal of Roentgenology and Radium Therapy* [Amer. J. Roentgenol.] 65, 420-458, March, 1951. 80 figs., bibliography.

### 516. The Action of Repeated Whole-body Irradiation with X Rays on the Blood and Haematopoietic Systems.

(Action des rayons X en irradiations totales itératives sur le sang et les organes hématopoïétiques)

J. DUCUING, P. MARQUÉS, and O. MILETZKY. *Journal de Radiologie, d'Electrologie, etc.* [J. Radiol. Electrol.] 31, 666-671, 1950. 3 figs., 1 ref.

From the Toulouse Regional Anti-cancer Centre the authors report the results of an experimental study of haematopoietic-tissue changes after whole-body x-irradiation in sublethal doses repeated over prolonged periods of time. A dog was first subjected to 4 annual courses of irradiation, consisting of thrice-weekly doses of 25 r to a total dose of 775 r per course in 2½ months. Regular haematological studies were carried out until the animal died at the 45th month, when necropsy and tissue culture of bone marrow were performed. Subsequently 3 guinea-pigs were severely exposed to the following doses: 400 r in 3 days, followed after 58 days by a further 400 r in 3 days; 500 r in 28 days, followed 92 days later by 25 r; and 500 r (single dose), followed in 80 days by a further 500 r. These animals died 90 to 110 days after the initial irradiation.

Details of the haematological findings tabulated and charted in the paper show that the early leucopenia, thrombocytopenia, and prolonged bleeding time, with later anaemia, were followed by various degrees of recovery. Latent haematopoietic depression was, however, manifest by each subsequent irradiation leaving the blood count more disturbed; there was summation of radiation damage and the lesions were partially irreversible. Ultimately the effects of successive irradiations culminated in the terminal syndrome of anaemia, leucopenia, thrombocytopenia, and haemorrhage, which might develop slowly, long after the last irradiation (being 5½ months afterwards in the case of the dog). Necropsy findings in the reticulo-endothelial system and other organs are correlated with the haematological changes.

Arthur Jones

### 517. The Effect of X-irradiation on Erythropoiesis, Plasma and Cell Volumes

J. FURTH, G. A. ANDREWS, R. H. STORY, and L. WISH. *Southern Medical Journal* [Sth. med. J. Bham, Ala] 44, 85-92, Feb., 1951. 7 figs., 10 refs.

Mice and rabbits were given LD50 doses of x rays. In rabbits there was a steady fall in the total erythrocyte mass for 9 days, followed by recovery. The plasma volume declined in the early stages and later rose. Routine blood counts thus did not reflect the true state of affairs in the circulating blood. In mice similar findings were noted.

A study of the reticulocytes in the peripheral blood suggested that erythropoiesis ceased within a day of the irradiation and failed to function for 12 to 14 days. *In vitro* erythrocytes are known to be resistant to x rays, but *in vivo* this may not be true. There is a rise in serum bilirubin concentration after irradiation, and massive erythrophagocytosis is seen. Evans blue, homologous plasma labelled with <sup>131</sup>I, and erythrocytes with <sup>32</sup>P all disappeared more rapidly in irradiated than in normal rabbits. The cannulated thoracic duct in dogs was found to discharge bloody lymph after x-irradiation of the animal, suggesting that an altered permeability of blood vessels allows the escape of erythrocytes into the lymph spaces. Colloidal gold injected intravenously into rabbits disappeared faster in irradiated than in normal animals. The absolute amount of <sup>198</sup>Au retained in the liver and spleen of irradiated mice was, however, the same as in controls, thus indicating no loss of function of macrophages.

John F. Loutit

### 518. Radiation Therapy of Carcinoma of the Vagina

F. BUSCHKE and S. T. CANTRIL. *Radiology* [Radiology] 56, 193-201, Feb., 1951. 10 figs., 7 refs.

Attention is drawn to the prevalent opinion that vaginal carcinoma is rare and difficult to treat, but figures are quoted from French sources and from the

authors' own Institute in the Swedish Hospital, Seattle, showing that a good proportion of patients are well 3 years after treatment—16 of 31 and 6 out of 10 in the two series treated. A method of staging is proposed and details of the methods of treatment are given. Two of the patients who remained well had had hysterectomy many years before, and 2 had lesions on the posterior wall, one high up the left lateral wall, and the other in the right fornix. All who died had lesions on the anterior wall, 2 spreading round to the posterior wall. All were treated with radium and x rays, the latter in 8 cases at 800 kV and in 2 at 200 kV. Success is thought to be due to adequate treatment of the lymph-drainage area by the x-ray therapy. Way (*J. Obstet. Gynec.*, 1948, **55**, 739) is quoted to show that the patients who survived for long periods were those with lesions in the upper third of the vagina, where a fairly standard radium application is possible. Low lesions failed to heal. Difficulties are overcome by carefully planned external x-ray therapy of the whole vagina followed by suitable radium therapy of the remaining central portion of the tumour. The method is illustrated by diagrams showing the position of the tumour in each case. [Although it is claimed that the use of very high voltage is not essential, it is obvious that the availability of 800 kV must have facilitated the delivery of the required dose to lesions situated within the pelvic outlet.]

M. C. Tod

## RADIODIAGNOSIS

519. A Study of Pneumoencephalograms before and after Prefrontal Lobotomy (Freeman-Watts Technic) I. MESCHAN and J. B. SCRUGGS. *Radiology* [*Radiology*] **56**, 222-227, Feb., 1951. 3 figs., 7 refs.

In a series of 19 psychotic patients pneumoencephalograms, made before and after prefrontal leucotomy, were studied and compared by the authors. The ages of the patients ranged from 24 to 66 years, and in all but one, where it was 9 months, the duration of the psychosis exceeded 3 years. There was no form of therapeutic procedure between the time of the pre-operative encephalography and the leucotomy.

In 14 cases the pre-operative encephalograms revealed normal ventricles, but in 5 of these the cortical sulcal markings were accentuated. Following leucotomy all 14 cases showed a significant absence of air in the subarachnoid space surrounding the brain, and with 4 exceptions, where they remained of normal size, the ventricles were diffusely dilated. In the 5 remaining cases of the 19 studied pre-operative encephalography revealed diffuse or localized ventricular dilatation. Post-operatively, 4 showed frontal porencephalic cysts, the occurrence of which may be explained by the fact that the anterior horns of dilated ventricles are more easily penetrated by the leucotome at operation. Progressive ventricular dilatation and obliteration of the cortical subarachnoid space was also found.

The ventricular dilatation is ascribed to a combination of cerebral atrophy and gliosis and to diminution of the

absorptive function of the arachnoid granulations. Obstruction to the free egress of spinal fluid between the basal cisterns and cortical subarachnoid space may be a contributing factor.

The findings in 6 necropsies from a series of 85 cases in which leucotomy had been performed included arachnoidal thickening, cortical atrophy, ventricular dilatation, and degenerative changes in the basal ganglia and in the nucleus medialis dorsalis of the thalamus.

R. G. Reid

### 520. The Normal Cerebral Angiogram

R. W. CURRY and G. G. CULBRETH. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **65**, 345-373, March, 1951. 31 figs., 23 refs.

### 521. Angiographical Diagnosis of Carotid Body Tumours. [In English]

H. IDBOHRN. *Acta Radiologica* [*Acta radiol., Stockholm*] **35**, 115-123, Feb.-March, 1951. 4 figs., 8 refs.

### 522. Patterns of Lobar Collapse as Observed Radiographically

M. LUBERT and G. R. KRAUSE. *Radiology* [*Radiology*] **56**, 165-182, Feb., 1951. 18 figs., 7 refs.

Attention is drawn to the lobar patterns which may be seen on a radiograph when different lobes of the lung are collapsed. Not only does the pattern vary with the lobe involved, but each individual lobe may show a differing appearance according to the degree of collapse and the presence or absence of previous intrapulmonary or pleural disease. Some of these varying appearances are illustrated.

The authors, however, claim that the basic appearance is sufficiently constant to allow certain generalizations to be made. Thus in collapse the lobe does not become a smaller replica of itself. Instead, there is a rather important change in shape. The usual three-dimensional pyramidal or conical configuration is replaced by a flattened triangle with the apex at the hilum, thus approaching a two-dimensional figure. The broad part of this triangle follows the curve of the parietal pleura with the base (the interlobar septum) lying against the lateral chest wall. As this process of collapse proceeds, the triangular mass becomes smaller and flatter. The apex of the triangle necessarily remains fixed at the hilum, so that the remainder of the lobe flattens against the mediastinal and parietal pleura and the base moves toward the hilum along the curved course of the chest wall.

L. G. Blair

### 523. Factors Influencing the Mediastinal Shadow in Young Children

F. H. KEMP. *British Journal of Radiology* [*Brit. J. Radiol.*] **23**, 703-709, Dec., 1950. 16 figs., 5 refs.

A study was made of serial radiographs of the chests of over 700 ostensibly normal children at the Institute of Social Medicine, Oxford. Experiments were also carried out in the post-mortem room. The author points out that the mediastinal shadow in young children is a

composite one made up of the heart and great vessels, the thymus, and groups of lymph nodes. This leads to a very wide range of normal appearances determined by the balance between the intra-pulmonary pressure and the resistance afforded by the degree of cardiovascular filling. Extraordinary effects are often seen, particularly if the child struggles or cries. The thymus gland plays an important part in the formation of the mediastinal shadow and it is extremely difficult to differentiate its form from the other structures. The most reliable indication of its whereabouts, occasionally observed, is a notch or triangular projection—rendered more obvious if the child is slightly rotated—which represents the lower pole. Subsequent radiographs of these children show that this shadow gradually recedes towards the mediastinum as the thymus gland is pressed backwards by the expanding lungs, which do not completely fill the bony cage in infancy but progressively increase in size as the child grows older. The shadow of the thymus gland may simulate or mask pulmonary pathology and congenital cardiac lesions. Owing to the presence of the thymus it is difficult to determine the size and accurate outline of the heart in young children, and in describing a radiograph it is better to refer to the "cardio-mediastinal shadow" than to the "heart shadow".

G. A. Stevenson

**524. The Clinical Picture of Bronchial Insufficiency. Observations on the Active Behaviour of the Lungs during Respiration.** (Das Krankheitsbild der Bronchial-Insuffizienz. Ein Beitrag zum aktiven Verhalten der Lungen bei der Atmung)

K. HECKMANN. *Fortschritte auf dem Gebiete der Röntgenstrahlen [Fortschr. Röntgenstr.]* 74, 23-39, Jan., 1951. 21 figs., 23 refs.

The various segments of the lung participate unequally in the normal process of respiration. Three types of lung ventilation are distinguishable—cranial, caudal, and general. These types can be differentiated by observing the changes in luminosity of the tissues on the radioscopic screen, the movements of the horizontal interlobar fissure, and bronchial spreading (by tomography). In cases in which the oxygen requirements of the blood are suddenly increased, all the bronchial segments enter into respiration; this corresponds to the establishment of "second wind". Diseased regions of the lung are excluded from this general response by a reflex spasm of the bronchi. Acute bronchial insufficiency leads to development of cavities, while chronic bronchial insufficiency leads to pulmonary emphysema.

A radiographic test of lung function is described, based on the compressibility of the lung.

A. Orley

**525. Angiopneumography and Bronchial Carcinomata. (Angiopneumographie et cancers du poumon)**

P. SANTY, M. BÉRARD, J. PAPILLON, and J. C. SOURNIA. *Journal Français de Médecine et Chirurgie Thoracique [J. franç. Méd. Chir. thorac.]* 5, 1-9, 1951. 8 figs.

Following the early attempts at angiopneumography by Egas Moniz and Lopo de Carvalho in 1931, angi-

pneumography according to the technique of Ravina and d'Ameuille became more popular, especially when a simple technique was elaborated by Robb and Steinberg and innocuous media opaque to x rays were available. In the first 6 months of 1950 the authors radiographed the large mediastinal vessels in 150 patients with various abnormalities or pulmonary affections. They discuss 40 cases of pulmonary carcinoma in which 90 pulmonary angiographs were carried out. The technique now used is very simple: after exposing a vein, usually the cephalic, at the elbow they inject 60 ml. of diodone (70%) at various rates, generally in not more than one second.

A sensation of great heat is often felt by the patient, and diffuse flushing appears. Tests for sensitivity to diodone show that about 1 in 5 patients are unsuitable for examination. An intravenous injection of 10 mg. morphine is given immediately before the diodone. This increases tolerance and prevents coughing, which would spoil the value of the radiographs. After the injection, 4 radiographs are obtained at intervals of one second.

Tumours at the periphery, though rare, are particularly difficult to diagnose for several reasons: such tumours are not amenable to bronchoscopy, radiography and tomography are often misleading; and transparietal puncture is not without danger. But angiopneumography shows distortion or compression of pulmonary arteries of the second or third order. With hilar tumours a simple compression of a pulmonary artery or one of the second order may be found; the vessel may be narrowed and sometimes even a complete obliteration may be present.

[This interesting article deserves study in full. The results of further work will be awaited with great interest.]

Geo. Vilvandré

**526. Angiocardiographic Findings in Thoracoplasty, Artificial Pneumoperitoneum, and Phreniclasia**

H. I. MCCOV, I. STEINBERG, and C. T. DOTTER. *Journal of Thoracic Surgery [J. thorac. Surg.]* 21, 149-158, Feb., 1951. 7 figs., 24 refs.

Using "neo-lopax" (75%) or diodone (70%) injected into an antecubital vein, the authors made angiograms of 17 patients with thoracoplasty, pneumoperitoneum, or phrenic paralysis. Diminished vascularity was seen in all, proportionate to the degree of collapse. Displacement and rotation of the heart and great vessels was demonstrated in the pneumoperitoneum group.

Geoffrey Flavell

**527. A New Angiocardiographic Sign of Patent Ductus Arteriosus**

R. H. GOETZ. *British Heart Journal [Brit. Heart J.]* 13, 242-246, April, 1951. 3 figs., 6 refs.

A new sign in the angiocardiographic diagnosis of patent ductus arteriosus is demonstrated. It consists of a defect in the homogeneous filling with the opaque material of the main pulmonary artery. It is brought about by the injection of blood from the aorta through the ductus diluting the opaque medium as it passes through the pulmonary artery.—[Author's summary.]

## 528. Calcification in the Patent Ductus Arteriosus

H. RUSKIN and E. SAMUEL. *British Journal of Radiology* [Brit. J. Radiol.] 23, 710-717, Dec., 1950. 7 figs., 12 refs.

A description is given of 4 cases in which calcification in a patent ductus arteriosus was demonstrated radiographically. The authors discuss the differential diagnosis of this from 12 other causes of calcification in this region. In the 4 cases described, the calcification was seen as a curvilinear shadow lying between the aortic knob and the pulmonary arc. It was best demonstrated by taking coned-down, overpenetrated teleradiographs under fluoroscopic control as described by Sosman (*Amer. J. Roentgenol.*, 1943, 1, 461). Tomography was not considered to be of great value since the comparatively long exposures required would fail to demonstrate minor degrees of calcification. The calcifications showed simultaneous movement with the pulsation of the aorta and pulmonary artery. In one case, in which the patent ductus was ligated, the calcification was palpated and found to be situated in the aorta at the attachment of the ductus. A Michel clip was placed at the aortic end to help to determine the exact site of the calcification radiographically. In the other 3 cases, in which a similar calcification was seen, a diagnosis of patent ductus was established clinically but the patients' lack of disability rendered surgical intervention unnecessary. Regarding the differential diagnosis, an aortic calcification is likely to cause confusion, but this is extremely rare in young adults and the arc of calcification is larger. It should also be remembered that calcification at the aortic end of an obliterated ductus does occasionally occur.

G. A. Stevenson

## 529. The Examination of the Abdominal Organs by Transverse Axial Stratigraphy after Retroperitoneal Insufflation in Children. (Stratigrafia assiale transversa per lo studio degli organi addominali dopo insufflazione retroperitoneale nel bambino)

G. SANSONE and A. DE MAESTRI. *Minerva Medica* [Minerva med., Torino] 1, 137-139, Jan. 27, 1951. 10 figs., 5 refs.

The authors refer to the most interesting observations made by Valebona by means of transverse axial stratigraphy (T.A.S.) of the chest, thus permitting examination of the respiratory and the cardiovascular systems in three dimensions. A similar type of examination of the abdominal organs presents more difficulties owing to the homogenous opacity of most of them. These difficulties are, of course, also present in routine radiography of the abdomen, but may be overcome by the use of contrast media. For over a year the authors tried to find the most satisfactory medium to be used with T.A.S. Their original technique consisted of insufflation of the stomach and colon. Later, they employed intravenous pyelography to outline kidney shadows. However, the authors admit that none of these methods produced the desired result. Pneumoperitoneum was also employed, with the patient placed in the erect position. This gave satisfactory results as far as the proximal abdominal organs are concerned, such as the liver and spleen.

The authors persevered in their search for a better technique and employed "retropneumoperitoneum" following the suggestion of this method by De Gennes, May, and Simon (*Pr. méd.*, 1950, 58, 351). This appeared to yield the best results. (The term "retroperitoneal insufflation" is preferred to the artificial "retropneumoperitoneum".) The introduction of gas, preferably oxygen, into the retroperitoneal space is performed by the introduction of a cannula into the soft tissue immediately in front of the os coccyx. The pressure of oxygen forces the peritoneum between the parenchymal organs, giving the desired contrast and outlining them. Distribution of the gas changes very little with changes in position of the patient.

Two cases are reported, one normal and one pathological (splenomegaly); a few interesting radiographs are reproduced, but investigations are still in a preliminary stage.

L. G. Capra

## 530. Evaluation of Aortography in Abdominal Diagnosis

L. R. SANTE. *Radiology* [Radiology] 56, 183-192, Feb., 1951. 11 figs., 23 refs.

For the purpose of aortography 20 ml. of 70% diodone is injected through a 15-cm. No. 12-gauge unbreakable needle into the aorta above the level of the last thoracic branch. The high site of injection is chosen to avoid the risk of introducing the total quantity of solution directly into the mesenteric vessels. The injection is given and the exposure made with the patient in the prone position. The skin is punctured just below the 12th rib and four fingerbreadths to the left of the spinous processes. The 15-cm. needle, with the stylet in position, is then directed anteriorly, medially, and upwards towards the body of the 12th thoracic vertebra. When the bone is encountered, the needle is withdrawn about 2 cm. and pointed more laterally, so as to pass close by the vertebral body. The stylet is withdrawn and the needle advanced until it enters the aorta. The operator feels a distinct sense of resistance as the needle penetrates the aortic wall, and almost immediately a pulsating drip will come from the needle. A trial injection of 12 ml. saline solution within 6 seconds is made in order to estimate the force required. The syringe containing the diodone is then connected and, following a test withdrawal of blood as a final proof that the needle is well within the lumen, the injection is made at the rate of 2 ml. per second. The first film is taken as the final 2 ml. is leaving the syringe. Immediately after the exposure of this film the needle is withdrawn. Another film is taken 2 or 3 seconds later to demonstrate the venous return.

The procedure is performed under thiopentone anaesthesia after premedication with morphine and atropine. When the injection of the dye is completed and the films taken, 1 litre of 5% glucose in normal saline solution is injected through the anaesthetic needle. When the blood supply to the pelvic organs is to be investigated, pressure cuffs are placed about the thighs and inflated to 200 mm. Hg pressure. The contraindications are similar to those for injection of the same materials into the circulation in other procedures, such as intravenous

urography or arteriography. It is also advised that the iodine sensitivity of the patient should be ascertained before the diodone injection.

The examination is of considerable value in determining the blood supply to the kidneys in cases of congenital abnormality of the kidney, in hydronephrosis, and in cases of ureteral blockage with resulting lack of function of the kidney, and also in the demonstration of aberrant vessels. It is thus useful in deciding the extent, nature, and the advisability of operation in any of these conditions. In vascular hypertension it will demonstrate any ischaemia of the renal circulation. It is useful in the differentiation of a renal neoplasm from a cyst. The neoplasm shows vascularity throughout, with "laking" of the blood supply within the tumour, which will be demonstrated in the second film. The cyst has thin, widely divergent blood vessels at the periphery and an avascular centre. In renal haematuria where the pyelogram appears normal a small renal cortical tumour may be demonstrated by aortography. In pregnant women the site of the placenta can be well demonstrated by the "puddling" of the circulation shown in both films. Finally, it is useful in certain conditions to show the level of a block in arteries of the lower limbs and pelvis.

L. G. Blair

**531. Relationship of the Nature of the Opaque Medium to Small Intestine Radiographic Pattern**

G. M. ARDRAN, J. M. FRENCH, and E. H. MUCKLOW. *British Journal of Radiology [Brit. J. Radiol.]* 23, 697-702, Dec., 1950. 4 figs., 10 refs.

The authors compared the effect on the mucosal pattern of the small intestine, as shown radiographically, of two forms of barium meal: (1) A simple suspension in water of barium sulphate. (2) A gel-colloid preparation of barium sulphate ("raybar"). In the laboratory the former flocculated in mucus, whereas the latter was non-flocculable. Normal subjects were examined, together with 7 cases of idiopathic steatorrhoea. All the subjects were first given simple barium sulphate suspension and films were taken showing the small intestinal pattern. After a short interval the non-flocculable raybar was given and films were again taken. If the interval was more than a few days a further control, with the simple suspension, was carried out. In normal subjects there was virtually no difference in the appearance of the small intestine as seen after simple barium sulphate and raybar, the pattern being detailed and feathery in both instances. In cases of steatorrhoea, however, the mucosal pattern was lost when the simple suspension was used, the contrast medium appearing as flocculated irregular clumps, but with raybar the detailed mucosal pattern was visualized as continuous columns with no evidence of flocculation or clumping. The difference in pattern is thought to be due to the type of suspension and not to changes in the clinical state. Where evidence of the flocculated (deficiency) pattern is sought, simple suspensions only should be used, while complex suspensions like raybar should be used whenever maximum mucosal detail is required.

G. A. Stevenson

**532. A Simple One-stage Method of Double-contrast Study of the Colon**

R. D. MORETON, E. M. COOPER, and E. F. FOEGELLE. *Radiology [Radiology]* 56, 214-221, Feb., 1951. 7 figs., 7 refs.

The authors consider that a double-contrast technique is essential for satisfactory radiological investigation of the colon. They claim that the method they describe takes no longer and is no more uncomfortable to the patient than a simple barium enema. It avoids the delay while barium is drained and evacuated from the colon which is the chief disadvantage of the usual two-stage double-contrast technique. Besides being time-consuming, this delay will completely spoil the examination if unduly prolonged. Any conventional enema apparatus is suitable if a metal Y-tube is inserted between the lower end of the rubber tube and the rectal tube and a hand insufflator attached to its free arm.

A barium mixture incorporating a suspending agent is run in slowly as far as the splenic flexure under screen control. The head of the table is then lowered, the patient turned towards the left, and injection of air is commenced. Progress is observed fluoroscopically and the patient is positioned so that barium drains from the lower colon towards the caecum. Should the distal colon overfill, the barium may be redistributed by turning the patient on to the left side. If a ("bardex") self-retaining type of catheter is used, a careful watch must be kept so that injection of air may be stopped immediately if obstruction is encountered, as otherwise dangerous overdistension may occur. This cannot happen with an ordinary catheter.

Immediately the bowel is outlined satisfactorily, films are taken with a high kilovoltage and a short exposure (90 kV, 15 mA seconds, at 40 inches (1 m.) with grid for an average patient). It is essential to obtain both prone and supine views, preferably stereoscopic. Occasionally additional films before and after evacuation, with the patient rotated under screen control, are needed to show the sigmoid colon and rectum.

Adequate preparation is vital. Fictitious polypi are the commonest difficulty encountered—these can be very confusing and occasionally the examination has to be repeated to elucidate the findings.

J. A. Shiers

**533. Intussusception of the Terminal Ileum and its Radiological Examination. (Les invaginations intéressantes la terminaison iléale et leur examen radiologique)**

M. FÈVRE. *Journal de Chirurgie [J. Chir., Paris]* 67, 1-25, Jan., 1951. 9 figs.

As an aid to the diagnosis of intussusception in children, x rays must be used with the greatest caution. Clinical findings must always have pride of place, and a negative radiograph may be disregarded. Five types of intussusception occur in this region: the ileo-colic, the ileo-caecal, the ileo-ileac, the ileo-ileac developing into the ileo-colic, and the ileo-ileac developing into the ileo-caecal. The ileo-ileac is the rarest and the most dangerous of all. Clinical findings are often minimal, radiological features are almost invariably absent except for the features common to all acute obstructions,

and gangrene occurs extremely rapidly owing to the poor blood supply of this area. The classical cup, cockade, or lobster's claw deformities are most frequently seen in the ileo-caecal and ileo-colic varieties. These signs are often very fleeting and visible only on the screen. An ileo-ileac intussusception will sometimes cause a filling defect on the inner side of the caecum or will drag the caecum over to the left, giving a fish-hook appearance. Extreme caution must be exercised in accepting radiological evidence of reduction after conservative treatment. After complete filling of the caecum an ileo-ileac intussusception may still remain, and the medium must be seen to pass along the ileum without distortion. No matter what the x-ray appearance, the persistence of symptoms always calls for surgery. A series of 15 cases is described, in all but one of which operative treatment was employed. The danger of incomplete reduction and the frequency of associated pathology make conservative treatment rarely justifiable.

R. T. Burkitt

534. **Portal Angiography at Operation for Banti's Syndrome.** (Portographies per-opératoires pour syndrome de Banti)

P. SANTY and P. MARION. *Presse Médicale* [Pr. méd.] 59, 221-223, Feb. 21, 1951. 9 figs.

During operations for portal hypertension the authors regularly perform portal angiography. Their technique is to tie the splenic artery, isolate the splenic vein, and tie a firm catheter into it. Through this, 40 to 50 ml. of 50% diodone is injected and a radiograph is taken. By this technique the whole of the intra- and extra-hepatic portal tract is outlined. The authors have used it in 15 cases of so-called Banti's syndrome, in 10 of which it was shown that the syndrome was due to an extra-hepatic block of the portal system. The block was due either to thrombosis of the portal or the splenic vein or to a post-inflammatory stricture of the portal venous system. A few were due to congenital strictures. Only 5 cases were associated with cirrhosis and intra-hepatic block.

This technique is of value in deciding the correct operation for each particular case—lieno-renal anastomosis or porta-caval shunt.

F. B. Cockett

535. **Liver and Spleen Visualization by a Simple Roentgen Contrast Method**

S. ZELMAN. *Annals of Internal Medicine* [Ann. intern. Med.] 34, 466-478, Feb., 1951. 8 figs., 13 refs.

The author outlines various radiological methods which have been used in the attempt to show the shape, size, and position of the liver and spleen, including plain film, barium, pneumoperitoneum, and intravenous injection of thorotrast. Of these, pneumoperitoneum gives the most successful results, but should be used only in selected cases; the dangers of thorotrast are well known.

A simple, relatively harmless procedure is here described which, in over 140 examinations, caused no ill effects apart from a mild abdominal discomfort of short duration; gastro-intestinal bleeding and perforation are

considered the only contraindications. The patient is given the two parts of a Seidlitz powder separately, dissolved in water, and is asked to retain the stomach gas until a radiograph has been taken. The drink is followed by rectal injection of air into the colon until the patient is aware of a feeling of fulness. X-ray examinations are made with the patient erect, using the postero-anterior view for the liver visualization, and the 30-degree left anterior oblique view for the spleen. The films are exposed at 40 in. (1 m.) focus-film distance in the expiratory phase, using a Potter-Bucky grid.

The author found poor correlation of clinical palpability with actual enlargement of the liver and spleen. Emphysema was often a factor in those cases where organs of normal size were considered clinically to be enlarged. Two main anatomical types of spleen were found: (1) the horizontal, and (2) the lateral; the horizontal is difficult to palpate even when enlarged, whereas the lateral may be palpated even when normal.

Sidney J. Hinds

536. **The Normal and Pathological Gall-bladder as Seen at Laparoscopic Cholangiography.** (Le choledoque normal et pathologique vu à la cholangiographie laparoscopique)

M. M. ROYER. *Archives des Maladies de l'Appareil Digestif* [Arch. Mal. Appar. dig.] 40, 53-62, Jan., 1951. 9 figs., 5 refs.

A series of 7 cases is briefly presented to illustrate the author's technique of injecting a water-soluble opaque dye directly into the gall-bladder through a laparoscope. The five references in the bibliography are all to papers by the author, the first paper having been published in 1942.

[The differential diagnosis between carcinoma of the head of the pancreas and an impacted stone is not completely reliable and, as the method is not free from danger, it has failed to replace exploratory laparotomy.]

Denys Jennings

537. **The Roentgen Appearance of the Central Fat Tissue of the Kidney: its Significance in Urography**

F. WINDHOLZ. *Radiology* [Radiology] 56, 202-213, Feb., 1951. 9 figs., 3 refs.

The central fat tissue of the kidney is seen in radiographs as an irregular, fan-shaped translucency within the renal outline. It shows best during the early stages of excretory pyelography, when contrast medium in the tubules makes the parenchyma more dense. Tomography may be needed to show it and distinguish it from bowel gas.

The amount of fat is increased in obesity, pressing upon and compressing the calyces and pelvis so that they seem elongated and empty as in "spastic" kidney. Similar changes are seen in diffuse atrophy of the parenchyma, but in this condition there is also narrowing of the parenchyma. Sometimes proliferation of fat completely compensates for the retraction of the parenchyma, so that the external dimensions of the kidney are unchanged. This condition, which the author names "central atrophy", can be detected only if the central fat is visualized.

Localized proliferation of fat is usually secondary to cicatrization of the parenchyma, but very occasionally occurs spontaneously. It causes a local increase in fat translucency and corresponding calyceal compression. Unless the fat translucency is seen, the changes due to the primary form are indistinguishable from those due to other renal tumours. The most extreme degree of local proliferation is seen in chronic, calcified, inactive renal tuberculosis.

Renal tumours which cause calyceal deformity obliterate the fat shadow around the affected calyces. The demonstration of an uninterrupted layer of fat around a congenitally elongated calyx will differentiate it from one elongated by a renal neoplasm.

Demonstration of the fat shadow may be of value in the diagnosis and investigation of congenital abnormalities. A translucency may indicate the presence of a non-functioning ectopic kidney, while in fused, crossed ectopic, and horseshoe kidneys the shape of the fat shadow may indicate whether the fusion is parenchymal or capsular.

*J. A. Shiers*

### 538. Cysts of the Kidney

**H. C. OCHSNER.** *American Journal of Roentgenology and Radium Therapy [Amer. J. Roentgenol.]* 65, 185-199, Feb., 1951. 24 figs., 31 refs.

Cases of renal cyst admitted to the Methodist Hospital, Indianapolis, during the years 1944-8 were reviewed in an effort to obtain information which would aid in their differentiation from other lesions, particularly hypernephroma. Although certain criteria are helpful, none is infallible, and it is important to consider real malignancy whenever what appears to be a simple cyst is encountered. Conversely cysts, particularly of the haemorrhagic and multilocular varieties, may simulate hypernephroma in their radiological appearance. Most commonly, simple cysts are found in the lower pole of the kidney in the fifth and sixth decades, but they may occur at any age. Infection of the cyst is rare, but concomitant urinary infection is quite frequent. Calculi are occasionally encountered in both simple and calyceal cysts.

The plain film may show a rounded shadow arising from that of the kidney. Pyelograms may be normal, but usually variations exist which are, however, less pronounced than would be produced by a tumour of the same size; they consist of pressure effects on adjacent calyces, as evidenced by one or more of the following: (1) elongation; (2) dilatation; (3) displacement; (4) flattening; (5) abbreviation; (6) obliteration; (7) crescentic deformity, this last being a typical finding. In one case where the lesion was diagnosed post-operatively as extra-urinary, the author believes that elongation of the calyces should have given the correct interpretation.

Pressure effects on the pelvis may also occur. Calyceal cysts are small cortical cavities which communicate with a minor calyx and are situated just distal thereto. An early hydronephrosis with predominant involvement of one calyx, or a cortical abscess, may give a similar urographic picture. Multilocular cysts are apt to produce a bizarre deformity.

In the cases of polycystic disease haematuria and abdominal pain were the predominant symptoms. The marked deformity seen bilaterally in urograms was pathognomonic. Excretion pyelograms were usually adequate in the study of these cases, but polycystic disease with poor excretion may require retrograde examination.

The pyelograms in many of the cases are reproduced in the article.

*Sydney J. Hinds*

### 539. Barium Modification with Methocel

**M. M. MARKS.** *American Journal of Surgery [Amer. J. Surg.]* 81, 6-9, Jan., 1951. 8 figs., 5 refs.

This is a report of the use of methyl cellulose powder (2.5% by weight) added to barium sulphate to ensure a permanent suspension and to prevent the flocculation which usually occurs in the standard media used for barium meal and enema studies. The addition of methyl cellulose results in the easy passage of the barium as a soft curd and avoids the dangers of obstruction from concretions. Subsequent purgings are not required. The mixture adheres to the mucosa more readily and is of special value in barium-and-air contrast studies of the large bowel. It is claimed to be of great help in the diagnosis of the usually elusive solitary polyp, and in all lesions of the colon which may be normally obscured by overshadowing by redundant loops of large bowel.

*C. Patrick Sames*

### 540. Excretory Urography: a Clinical Trial of a New Contrast Medium (Sodium 3-acetylamino-2, 4, 6-triiodobenzoate)

**L. L. ROBBINS, F. H. COLBY, J. L. SOSMAN, and W. R. EYLER.** *Radiology [Radiology]* 56, 684-688, May, 1951. 6 refs.

An investigation into the comparative advantages and disadvantages of two intravenous contrast substances, sodium 3-acetylamino-2, 4, 6-triiodobenzoate ("urokon") and iodopyracet ("diodrast"), has been carried on for the past year. The results of 2,952 examinations have been analysed. In 1,537 of these urokon was the contrast substance and in 1,415 diodrast was used. Many more vasomotor reactions occurred with diodrast than with urokon, but approximately the same number of other minimal reactions were experienced by the patients in each group. No serious reactions, such as loss of consciousness, were noted in the urokon group; one occurred in the diodrast group. The diagnostic quality of the x-ray films was not appreciably different with the two media. Urokon appeared to be more rapidly excreted than diodrast.—[Authors' summary.]

### 541. Roentgenologic Examination of the Colon using Drainage and Negative Pressure, with Special Reference to the Early Diagnosis of Neoplasm

**F. E. TEMPLETON and E. A. ADDINGTON.** *Journal of the American Medical Association [J. Amer. med. Ass.]* 145, 702-704, March 10, 1951. 2 figs., 4 refs.

### 541 (a). An Evaluation of Translumbar Arteriography

**P. G. SMITH, T. W. RUSH, and A. T. EVANS.** *Journal of Urology [J. Urol.]* 65, 911-921, May, 1951. 8 figs., 23 refs.

## Pathology

### 542. The Role of Some Higher Peptides in Inflammation

W. G. SPECTOR. *Journal of Pathology and Bacteriology* [J. Path. Bact.] 63, 93-110, Jan., 1951. 2 figs., 13 refs.

Working at University College Hospital Medical School, London, the author studied the effect of intradermally injected peptic digest of fibrin on capillary endothelium in rats, having previously injected 1% trypan blue intravenously as indicator. It was found impossible to purify the crude fibrin digest by adsorption on charcoal. The active substance could be almost quantitatively adsorbed on Fuller's earth, but eluates contained only a small quantity of partly insoluble material, which was but slightly more active than the original digest. Purification was not achieved with cation-exchange techniques. It was found by paper partition chromatography and elution of the strips that all the activity was contained in the area occupied by the higher peptides, amino-acid spots being inert. All these experiments were made on the water-soluble fraction of the digest. The water-insoluble material made up about 10% of the dry weight of the digest. It was taken up into a fine suspension in strong alkali. Prolonged shaking with ethyl, methyl, and butyl alcohols produced a yellow solution, but it was most quickly extracted by a mixture of equal parts of ether and absolute ethyl alcohol. It had the same activity as the water-soluble fraction. From paper partition chromatography experiments it was concluded that the water-insoluble fraction consisted of the same substances as the water-soluble fraction, but bound together in some (possibly lipid) matrix.

The material active in the permeability test in the water-soluble fraction was completely precipitated by 75% saturation with ammonium sulphate. The precipitate was more active in regard to leucocyte emigration and capillary endothelial swelling than the crude digest. It consisted of peptides only. It was quantitatively adsorbed on Fuller's earth. It could not be purified by fractional precipitation with alcohol at 2° C. Under the influence of electrodialysis the fraction active in the capillary permeability test migrated to the cathode. The material which did not migrate in this way was found to produce increased capillary permeability, but its effect was masked by its vasoconstrictor effect in all but the highest dilutions. Iontophoresis at pH 4.0 failed to effect separation of the active principle.

The supernatant fluid from the ammonium sulphate precipitation was as active as regards leucocyte emigration and capillary endothelial swelling as was the precipitated material. The mean chain length of the peptide in the supernatant was 5 amino-acids, and in the precipitate 10. Acid hydrolysates of all the fractions mentioned contained tyrosine, phenylalanine, and leucine with or without isoleucine, valine, histidine, arginine, lysine,

$\beta$ -alanine, threonine, glycine, serine, and aspartic and glutamic acids. All but the supernatant from ammonium sulphate precipitation contained proline and amino-butyric acids. Tryptic digestion of the ammonium sulphate precipitate deprived it of its power of increasing capillary permeability, but not of attracting leucocytes or inducing capillary endothelium to swell. Injection of the antihistamine drug mepyramine practically abolished the capillary permeability effect without altering polymorph migration and endothelial swelling caused by the crude digest. Peptic digests of blood albumin and gelatin were active, as was the peptide, crystalline beef-pancreas-trypsin-inhibitor, all of these active substances being precipitated at 75% saturation with ammonium sulphate. Experimentally induced sterile inflammatory exudates from goats, rabbits, and guinea-pigs all showed activity. In experimental burns in anaesthetized rats increased permeability was apparent at once, reaching a maximum within 5 minutes. Leucocyte emigration and endothelial swelling appeared half to one hour later.

These results and the role of peptides in inflammation are discussed.

W. H. H. Merivale

### EXPERIMENTAL PATHOLOGY

### 543. The Effect of Foster Nursing on the Growth of a Transplantable Tumor

M. K. BARRETT and M. K. DERINGER. *Cancer Research* [Cancer Res.] 11, 134-138, Feb., 1951. 1 fig., 7 refs.

Previous work by the same authors (*J. nat. Cancer Inst.*, 1949, 10, 81) has shown that a transplantable mammary adenocarcinoma of mice grew at different rates in  $F_1$  hybrid hosts according to whether  $C3H \times C$  or  $C \times C3H$  hybrids received inoculations. A repetition and extension of these observations is now described, together with a study of the influence of foster-nursing from birth,  $C \times C3H$  mice being suckled by  $C3H$  foster mothers, and  $C3H \times C$  mice by their own mothers. The tumour used grows in all strain- $C3H$  mice and in all  $F_1$  hybrids with strain- $C$  mice, but does not grow in strain- $C$  mice. It has been shown to contain the mammary-tumour milk agent. Tumours were excised after 3 weeks and weighed, the findings being expressed as a ratio of the average tumour size in  $C \times C3H$  hybrids to that in  $C3H \times C$  hybrids. Results are shown graphically and were analysed statistically.

When both types of hybrid were suckled by their own mothers the difference in tumour growth rate was found as before. However, when hybrids with strain- $C$  mothers were foster-nursed by strain- $C3H$  mothers, no difference in growth rate was found. It is suggested that this finding cannot with certainty be attributed to the mammary-tumour milk agent.

H. G. Crabtree

**544. The Effect of Freezing and Freeze-drying on the Transplantation of Sarcoma 37**

P. T. J. C. P. WARNER and J. V. T. GOSTLING. *British Journal of Cancer* [Brit. J. Cancer] 4, 380-395, Dec., 1950. 4 figs., 24 refs.

The behaviour was investigated of minced mouse tumour (sarcoma 37) after rapid and slow freezing to a temperature below  $-75^{\circ}\text{C}$ ., repeated freezing and thawing, and freeze-drying. A modification of the freeze-drying technique of Craigie was used. Following treatment the tumour tissue, both undiluted and diluted in tenfold serial steps in physiological saline, was injected into mice, each animal receiving the same suspension of tumour tissue at 4 different sites. A qualitative method was employed to assess the results, based on the determination of the dose of tissue giving rise to tumours in 50% of the inoculated mice. Rapidly frozen tumour tissue induced fewer tumours than slowly frozen tissue. No tumours were observed in mice inoculated with either repeatedly frozen and thawed or frozen-dried material reconstituted in distilled water.

The results are presented as evidence of cell survival rather than the release of a virus from tumour cells following freezing and freeze-drying.

*L. Dmochowski*

**545. The Fate of Grafts of Sarcoma 37 Mince after Exposure to Low Temperature and Freeze-drying**

P. T. J. C. P. WARNER, J. V. T. GOSTLING, and A. C. THACKRAY. *British Journal of Cancer* [Brit. J. Cancer] 4, 396-404, Dec., 1950. 14 figs., 24 refs.

Minced sarcoma 37 tissue, untreated or previously subjected to rapid freezing, slow freezing to  $-75^{\circ}\text{C}$ ., repeated freezing and thawing, and freeze-drying, was grafted into mice. The grafts were taken out at intervals ranging from 3 hours to 10 days and serial sections examined. They showed early necrosis of nearly all cells, followed by infiltration of polymorphonuclear leucocytes into the grafts, and finally proliferation of fibroblasts and capillaries, at first in the surrounding tissues and then in the grafts. Characteristic large cells, designated "T" cells and considered to be surviving tumour cells, were seen at first at the periphery of the grafts and later in the surrounding tissues. The number of these characteristic cells in the grafts of untreated and rapidly or slowly frozen tumour tissue was roughly proportional to the tumour-producing activity of the material. These cells could not be found in the grafts of repeatedly frozen and thawed or frozen-dried tissues.

The authors conclude that transmission of tumours with frozen material is due to cells which survive the treatment.

*L. Dmochowski*

**546. Circulatory Responses to Variations in Intra-abdominal Pressure**

D. S. RIDLEY. *Journal of Pathology and Bacteriology* [J. Path. Bact.] 63, 17-32, Jan., 1951. 5 figs., 23 refs.

Experiments were performed in the Department of Morbid Anatomy, University College Hospital, London, on 80 rabbits, mostly males, weighing 1,500 to 2,500 g. Heparin was given before the experiments, and the

animals were lightly anaesthetized with pentobarbitone and ether. The intra-abdominal pressure was increased by injecting saline or air into the peritoneal cavity or the gastro-intestinal tract while an abdominal binder was loosely applied. Pressures in vessels and in the right auricle were measured by means of cannulae and cardiac catheters, while that in the portal vein was measured by insertion of a U-tube connected with a manometer. Diodone venography was performed and electrocardiograms were also obtained. A rise in the intra-abdominal pressure to about 50 mm. Hg caused a slight rise in the arterial pressure which was apparently abolished by elimination of sympathetic impulses, but not by section of the vagi. The right auricular pressure also rose during abdominal compression, while the heart rate decreased and the ventilation rate increased. There was also a flattening of the T wave in leads I and II. Except when the intra-abdominal pressure was high the pressure in the inferior vena cava rose with the abdominal pressure, but the venous blood flow distal to the renal veins was diminished or even reversed. The pressure in the portal vein was generally higher than in the vena cava, and radiographic observations suggested that communications between the inferior vena cava and the ascending lumbar veins were responsible for this difference, since they allowed blood from the inferior vena cava to escape from the abdomen. By a system of ligatures and subsequent washing of blood of the regions so separated an [approximate] idea was obtained of the way in which the blood was distributed in the body of some experimental animals, and it was concluded that the abdominal blood volume may not have fallen when the intra-abdominal pressure rose. This in turn led to the conclusion that active arteriolar dilatation may have taken place in the region of the abdomen when the intra-abdominal pressure was raised. It was further concluded that circulatory distress following a rise in intra-abdominal pressure is caused by interference with respiratory movements.

*E. M. Glaser*

**547. The Sequence of Circulatory, Respiratory and Cerebral Failure during the Process of Death; its Relation to Resuscitability**

H. G. SWANN and M. BRUCER. *Texas Reports on Biology and Medicine* [Tex. Rep. Biol. Med.] 9, 180-219, Spring, 1951. 2 figs., 36 refs.

This paper amplifies and completes previous studies by the authors on the same subject. Dogs were observed in the following states of anoxia: (1) while breathing pure nitrogen; (2) while breathing 2.43% oxygen in nitrogen; (3) while breathing 1% carbon monoxide; and (4) in obstructive asphyxia. In all experiments the induced anoxia served as the general anaesthetic.

The conclusion was reached that a critical circulatory change was most clearly indicated by the systolic blood pressure alone. Two limits of systolic blood pressure were defined, namely, the point at or above which oxygen insufflation uniformly succeeded in restoring circulation, and the point at or below which it uniformly failed to do so; the latter point was taken as the point at which "circulatory failure" had occurred. In all

4 types of anoxia studied these 2 levels were, in round figures, 100 and 50 mm. Hg respectively; thus circulatory failure was imminent when the systolic pressure fell to 100 mm. Hg, and it had actually occurred when the systolic pressure had fallen to 50 mm. Hg; below this point artificial respiration was futile, even though the dog were still breathing. This finding would appear to indicate that in the anoxic dog, and presumably in man too, artificial respiration, if it is going to be successful, should show sign of success within a few seconds of its commencement, that is, within the period (average 20 seconds) during which the systolic blood pressure falls from 100 to 50 mm. Hg.

In the anoxia of pure nitrogen the respiration consistently failed before the circulation failed. In the remaining three series, however, the breathing failed sometimes before, sometimes simultaneously with, and sometimes (in approximately one-third of the experiments) after, circulatory failure; this last finding is contrary to the generally accepted view that in anoxia the respiration invariably fails before the circulation; this "widespread misapprehension" is attributed to the use of general anaesthesia in such experimental studies.

In Series (1), (2), and (4), if the circulation was restored by oxygen insufflation before the point of circulatory failure, then the dog survived without any permanent cerebral damage; when attempts were made to push the anoxia beyond the point of circulatory failure (during a further 1 to 3 minutes) to a point at which resuscitation could be effective only by oxygen insufflation together with cardiac massage, fatal and irreversible cerebral damage did occur in the short-lived survivors. But in the dogs of the third series, which were poisoned with carbon monoxide, fatal and irreversible cerebral injury actually occurred before circulatory and respiratory failure; out of 29 of these dogs which were resuscitated at a time when the blood pressure and breathing were still quite strong in most of them, 22 died within 1 to 14 days from cerebral damage; this finding would appear to indicate that in this form of anoxia "resuscitation" may be needed even though the breathing and blood pressure are still good.

[Perhaps it should be stressed that what the authors mean by the term "circulatory failure" is a narrowly defined state of profound cardiovascular depression.]

Joseph Parness

**548. Observations Concerning the Production and Excretion of Cholesterol in Mammals. III. The Source of Excess Plasma Cholesterol after Ligation of the Bile Duct.**

S. O. BYERS, M. FRIEDMAN, and F. MICHAELIS. *Journal of Biological Chemistry* [J. biol. Chem.] **188**, 637-641, Feb., 1951. 11 refs.

After ligation of the common bile duct, rats exhibited a rapid and marked rise in the cholesterol content of their plasma. This increase consisted largely of free cholesterol. The rise could not be prevented by prior castration, adrenalectomy, viscerectomy, or ligation of the thoracic duct. Total hepatectomy and partial hepatectomy prevented this rise. Intravenous infusion

of choline, inositol, lecithin, or unchanged bile was unable to produce excess cholesterol in the partially hepatectomized animal. It is concluded that the liver itself discharges into the blood stream the excess cholesterol occurring in plasma after bile-duct ligation.—[Authors' summary.]

**549. Observations on Inhibition of Nucleic Acid Synthesis Resulting from Administration of Nitrogen Mustard, Urethan, Colchicine, 2:6-Diaminopurine, 8-Azaguaine, Potassium Arsenite, and Cortisone**

H. E. SKIPPER, J. H. MITCHELL, L. L. BENNETT, M. A. NEWTON, L. SIMPSON, and M. EIDSON. *Cancer Research* [Cancer Res.] **11**, 145-149, Feb., 1951.

By the use of labelled precursors it has been shown that formate, carbon dioxide, and glycine are fundamental units in the bio-synthesis of uric acid and of the nucleotides of ribose- and deoxyribose-nucleic acids. These findings prompted the authors to use labelled formate and carbon dioxide to measure the rate of nucleic acid formation in mice, and to study how this process is influenced by the diverse agents which have been shown to produce temporary palliative effects on some forms of cancer.

Sodium formate labelled with  $^{14}\text{C}$  was injected into groups of 4 adult strain-CFW mice. After 6 hours the viscera of 4 mice (and also those of 4 untreated mice) were homogenized and dehydrated with ethyl alcohol and ether. This material was extracted with 10% sodium chloride solution, and the crude sodium salts of the mixed nucleic acids were precipitated with alcohol and redissolved in water. The free nucleic acids were then precipitated with hydrochloric acid and alcohol, washed with water, and dried with alcohol and ether. From this product deoxyribose nucleic acid was separated by hydrolysis in 2N sodium hydroxide for two periods of 18 hours at room temperature, and precipitated with hydrochloric acid and alcohol. Another portion of the combined nucleic acids was hydrolysed in 0.5N hydrochloric acid for one hour and the purines precipitated with silver nitrate. Determinations of  $^{14}\text{C}$  were made on these fractions by a gas-phase procedure (J. biol. Chem., 1948, **173**, 371) and their activity expressed as  $\mu\text{c. per mol of carbon}$ . Similar experiments were carried out with  $^{14}\text{CO}_2$  (as  $\text{NaH}^{14}\text{CO}_3$ ) which is a less specific precursor of the 6-carbon atom of the purine skeleton. By estimating the activities 1, 6, and 24 hours after injection the rate of turnover of formate C in nucleic acids and their purine moieties was established, and little free radioactive formate or bicarbonate carbon was found in the tissues after 6 hours.

Anti-cancer agents were injected either as a single LD<sub>50</sub> dose or in six successive daily doses at the maximum tolerated level followed by a further LD<sub>50</sub> dose. Immediately after the last dose  $\text{H}^{14}\text{COONa}$  was injected, and after 6 hours the nucleic acids and purines were isolated by the above procedures.

The specific activities of viscera homogenate, combined nucleic acids, and combined nucleic acid purines for treated and untreated mice are given in tabular form. They show that 2:6-diaminopurine, 8-azaguaine,

cortisone, potassium arsenite, urethane, and nitrogen mustard all inhibit nucleic acid synthesis *in vivo*, whereas benzene and colchicine produce no inhibition.

H. G. Crabtree

**550. Effect of Experimental Shock Induced by *Clostridium perfringens* Toxin on the Kidneys of Dogs**

M. BERG, S. A. LEVINSON, and K. J. WANG. *Archives of Pathology [Arch. Path.]* 51, 137-153, Feb., 1951. 10 figs., 27 refs.

The authors, working at the Illinois University College of Medicine on the effect of experimental shock induced by *Clostridium perfringens* toxin on the kidneys of dogs, injected 8 mg. of the toxin per kg. body weight into the mid-portion of the hind leg of the dogs. The animals died in 5 to 6 hours. In a controlled series of 15 dogs the average blood pressure, taken hourly direct from the femoral artery, gradually fell. Decreasing amounts of urine were excreted, and none after 5 hours. Haemoconcentration occurred in the test animals only. The volume of the injected leg increased after 2 hours, and in the third hour it amounted to 2% of the body weight. Specimens of urine showed increasing amounts of casts, albumin, and cells. In test animals the urinary chloride content decreased in the first hour, but in the controls it remained normal for 3 hours. After 4 hours the blood urea level averaged 17 mg. per 100 ml. of blood in the controls and 25 mg. per 100 ml. in the test animals. The plasma chloride level fell slowly over 4 hours.

In a second experiment animals were killed at half-hourly intervals. Six minutes before death 1.0 mg. of phenol red, excreted mainly by the proximal convoluted tubules (P.C.T.), and 5 ml. of sodium ferrocyanide, excreted mainly by the glomeruli, per kg. was injected intravenously. The kidneys were frozen and dehydrated or fixed in formalin. Soon after receiving the toxin, the kidneys showed the changes seen in animals dying of shock. Two to 2½ hours after the injection about 50% of the glomeruli, and at 3 to 3½ hours a much larger number, were devoid of blood cells and appeared swollen: they contained little or no ferrocyanide. The P.C.T. showed damaged epithelium. At 4 to 4½ hours the glomeruli appeared shrunken and the P.C.T. showed severe damage. A considerable amount of ferrocyanide was seen in the more normal glomeruli and P.C.T. Hardly any phenol red was seen in the P.C.T. and only in an occasional epithelial cell.

In 4 animals the injected leg was encased in plaster. The blood pressure at each successive hour averaged 85, 67, 46, and 21% of the control value. There was slight haemoconcentration after 4 hours. Casts appeared in the urine after 2 hours, but output was normal for the first 4 hours. The serum levels of urea nitrogen and chlorides showed small changes only. Kidneys examined at 4 to 5 hours showed congestion and a few small areas of necrosis in the P.C.T. only. Ferrocyanide was usually present in normal amounts and phenol red was absent, or present in only minimal amounts. Three animals had the injected leg massaged: the blood pressure at each successive hour averaged 82, 82, 80, and 79% of the control value. Urinary output had fallen significantly after 1 hour and casts and cells were present; there

was gross blood-staining after 2 hours, and no urine at all after 4 hours. After 3 hours there was haemoconcentration and severe haemolysis. Sections after 4 hours showed swelling of glomeruli and haemoglobin in Bowman's space and in the P.C.T., which exhibited patchy, cloudy swelling and necrosis. Considerable amounts of ferrocyanide were seen in the more normal-looking glomeruli and P.C.T., but no phenol red.

The authors consider that the contraction of the glomerular capillaries towards the end of the first experiment was perhaps part of a generalized vasoconstriction to maintain blood pressure following a serious fall in blood volume due partly to oedema in the injected leg: they contrast this with the results of the plaster-cast experiment. The severe damage to the tubules in the massaged dogs was thought to be due partly to circulating toxins and partly to reabsorption of the haemoglobin excreted by the glomeruli following massive haemolysis. There seemed to be a correlation between the appearance of mitochondria in the P.C.T. and the excretion of phenol red. *Peter Harvey*

**551. Experimental Studies of Asbestosis**

A. J. VORWALD, T. M. DURKAN, and P. C. PRATT. *Archives of Industrial Hygiene and Occupational Medicine [Arch. industr. Hyg. occup. Med.]* 3, 1-43, Jan., 1951. 13 figs., 15 refs.

Animals were exposed to various asbestos dusts: (a) by inhalation for 2 to 5 years, 8 hours a day, in a chamber in which a dust cloud was maintained by a rotating paddle in a dust hopper; and (b) by intratracheal, intraperitoneal, and intravenous injection.

Inhalation of a commercial asbestos dust of mixed fibre length (1  $\mu$  to 1 mm.) produced peribronchiolar fibrosis in the lungs of guinea-pigs, but not in the lungs of rabbits or rats; the fibrosis did not progress significantly after exposure was stopped. A short-fibre dust, mainly of 3  $\mu$  or less but with a small admixture of longer fibre, produced a slower and less extensive fibrosis in guinea-pigs and white rats. Cats reacted with atypical subpleural fibrosis, and rabbits with only slight parenchymal fibrosis. To "100% ball milled dust" with still fewer long fibres it was found that the tissue reaction was even less intense, though more dust accumulated in the lungs and progression of the lesion was seen in some cases after removal from exposure. With exposure to a pure long-fibre chrysotile the tissue response was more rapid and intense in guinea-pigs, which also showed lymph-node fibrosis, while in cats peribronchial fibrosis appeared for the first time. Thus reduction of fibre size does not seem to increase the biological activity of asbestos as it does with silica, and the stimulus therefore seems to be mechanical rather than chemical. Simultaneous dusting with the asbestos dust and infection with tubercle bacilli appeared to produce local extension of lesions, followed by healing.

Intratracheal injection of various long-fibre asbestos minerals showed that all types except anthophyllite produced peribronchiolar fibrosis, as did the asbestos-like mineral brucite ( $MgO \cdot H_2O$ ), which contains less

than 1% free silica. Long-fibre chrysotile, ignited to destroy its flexibility, did not produce fibrosis; nor did non-fibrous serpentine of similar chemical constitution or glass-wool fibre of similar size. Injection confirmed that the short fibres of various minerals caused little or no fibrosis; this observation differs from those of King *et al.* (*Thorax*, 1946, 1, 188). Intraperitoneally, long-fibre dusts produced a fibrous reaction, though short fibres did not. After intravenous injection only phagocytosis of inert dust was seen.

Colloidal aluminium hydroxide added to the long-fibre chrysotile before intratracheal injection gave no protection. The iron coating of asbestos bodies derives from blood or tissue and not from mineral fibre: asbestos bodies recovered from human lungs are inert when injected into guinea-pigs.

These experiments show that tissue and species specificities are more marked for asbestos than for silica. The mouse and dog are not affected by asbestos dust. The authors suggest that the mechanical effects of long-fibre dusts are increased by the mobility of lung tissue. The minimum length of fibre to produce typical reaction is probably 20 to 50  $\mu$ .

[This long and important paper is based on some 20 years' experiments at the Saranac Laboratory.]

J. N. Agate

**552. Experimental Beryllium Granulomas of the Skin**  
F. R. DUTRA. *Archives of Industrial Hygiene and Occupational Medicine* [Arch. industr. Hyg. occup. Med.] 3, 81-89, Jan., 1951. 5 figs., 7 refs.

Pulmonary and skin granulomata occur in men exposed to certain beryllium compounds. An attempt was made to produce such lesions by implanting into skin samples of beryllium metal, two kinds of beryllium oxide calcined under different conditions, and two kinds of fluorescent powder containing beryllium oxide, of identical chemical composition but calcined differently. In rabbits and rats no lesions developed. The skin of pigs more nearly resembles that of man: the powder was therefore implanted into pigs' skin, together with various control implants, and biopsies were taken at intervals from 2 days to 6 months. The initial wounds healed spontaneously. Tissue reactions occurred in the subcutaneous fat immediately below the dermis. Beryllium metal and the two oxide samples produced foreign-body reactions of non-specific granulomatous type. The two fluorescent powders produced the typical whorled, collagenous granulomata seen in human berylliosis. The powder calcined for a shorter time at lower temperature gave the more extensive and prolonged reaction. This may have been due to increased solubility of beryllium oxide and to the higher surface: weight ratio of its particles.

J. N. Agate

**553. Osteogenic Sarcoma after Inhalation of Beryllium Oxide**

F. R. DUTRA, E. J. LARGENT, and J. L. ROTH. *Archives of Pathology* [Arch. Path.] 51, 473-479, May, 1951. 2 figs., 11 refs.

M—L

**554. The Effect of A.C.T.H., Cortisone, and D.C.A. with Ascorbic Acid on "Formalin-arthritis"**

M. W. PARKES, and F. WRIGLEY. *British Medical Journal* [Brit. med. J.] 1, 670-675, March 31, 1951. 7 figs., 7 refs.

It was asserted by Selye in 1949 that adrenocorticotrophin (ACTH) and cortisone would prevent the acute and chronic stages of experimental "formalin arthritis", having in this respect an opposite type of action to deoxycortone acetate (DCA), which exacerbated this condition. He also asserted that the lesions of "formalin arthritis" microscopically resembled the rheumatic-fever lesion in the acute stage, and the rheumatoid lesion in the chronic stage.

The authors of this paper record their experience with "formalin arthritis" in the rat, employing an ingenious method of their own devising for evaluating changes in limb volume. Their results do not confirm Selye's statement that a "self-maintaining chronic inflammatory process" develops in the ankle-joint, showing "little or no sign of regression for weeks after the last injection". They frequently found that the limbs of their rats had returned to normal, or nearly so, by the end of 4 weeks, although histological examination did usually reveal some residual abnormality. Nor did their observations support the claim that DCA and ascorbic acid can prevent the development of "formalin arthritis"; indeed in every case this combination exacerbated the acute oedematous response of the foot, which they also observed in animals treated with DCA alone. Neither cortisone nor ACTH had any effect on the swelling of the foot, nor did they appear to exert any protective action against "formalin arthritis".

As a result of their experiments, which are described in detail, they conclude that "formalin arthritis" for use is unsuitable in a screening test for substances proposed for the treatment of the rheumatic diseases.

W. S. C. Copeman

## MORBID ANATOMY

**555. The Choroid Plexus in Tuberculous Meningitis. (Les plexus choroides de la tuberculose méningée)**  
L. BERTRAND and J. SALVING. *Presse Médicale* [Pr. méd.] 59, 230-233, Feb. 21, 1951. 16 figs., 18 refs.

In a study of the choroid plexus in cases of tuberculous meningitis treated with streptomycin, lesions were found in 15 out of 20 cases. Lesions in neighbouring structures were frequent, in 2 cases with no involvement of the plexus. Apparently banal inflammatory lesions were the most frequent, and lympho-histiocytic infiltration of a variable number of digitations was found, sometimes involving only a part, in others the whole, with deformation. In 8 cases specific lesions with giant cells and caseation were found, with rupture of the epithelium. Non-specific lesions, with swollen digitations and epithelium broken in places, appeared to be caused by an interstitial oedema. In 3 cases a coincident lesion with polymorphonuclear infiltration was the sequel to intraventricular injections of streptomycin. Tuberous bacilli were found only once.

Involvement of the plexus may be the result of a haematogenous invasion in cases of generalized tuberculosis. In 11 cases in the present series there was internal hydrocephalus, and in 16 basal caseation; in 4 hydrocephalic cases there were no plexus lesions. The plexus may be secondarily invaded by a virulent meningitic infection.

Gwenron M. Griffiths

**556. Allergic Granuloma of the Lung. Clinical and Anatomic Findings in a Patient with Bronchial Asthma and Eosinophilia**

J. C. EHRLICH and A. ROMANOFF. *Archives of Internal Medicine [Arch. intern. Med.]* **87**, 259-268, Feb., 1951. 9 figs., 16 refs.

A man aged 49 suddenly became ill with dyspnoea, cough, and wheezing. His condition was diagnosed as due to bronchial asthma and treated with adrenaline, at first with success. The episodes of bronchial spasm became more frequent and severe, small amounts of tenacious sputum were raised, cyanosis increased, and the patient was finally admitted to hospital, where he lapsed into coma and died on the tenth day of illness. Though no breath sounds were heard and no movements of the chest wall could be seen, a few rales and rhonchi were audible over both lungs; cerebral anoxia secondary to tracheo-bronchial obstruction was diagnosed. The leucocyte count was 16,200 per c.mm., with 68% polymorphonuclear leucocytes, 22% lymphocytes, and 10% eosinophils. The patient had suffered from hay fever.

At the necropsy the tracheobronchial tree was completely filled by a rubbery, mucopurulent cast, which was shown histologically to extend into the bronchioles and to contain many eosinophils and polymorphonuclear leucocytes; culture yielded haemolytic streptococci and *Haemophilus influenzae*. Foci of eosinophils were found histologically in the epicardium, stomach and small gut, bone marrow, spleen, lymph nodes, and diaphragm. Apart from the tracheobronchial cast the most remarkable feature was the finding in the left upper lobe of a spherical mass, 5 cm. in diameter, with an overlying fibrinous pleurisy; there was a similar, smaller mass in the upper lobe of the right lung. These masses were firm; on histological examination a dirty yellow central necrotic portion was seen, surrounded by a densely cellular inflammatory zone sharply separated from the surrounding lung. The necrotic centre contained many areas staining pink with eosin and consisting of innumerable eosinophil "corpses" and their granules. The structure of the inflammatory zone was typical of an allergic granuloma.

The authors suggest that had the patient lived, a diagnosis of Loeffler's syndrome would have been made. They review briefly the relationship between pulmonary allergic granulomata, eosinophilia, and allergic changes in other organs, and point out that Loeffler's syndrome is essentially a systemic disturbance, too often regarded only as an evanescent lung condition. A transition can be traced from Loeffler's syndrome on the one hand to widespread allergic granulomatosis or periarteritis nodosa on the other.

Maxwell Telling

**557. Pathology of the Pulmonary Vascular Tree. II. The Occurrence in Mitral Insufficiency of Occlusive Pulmonary Vascular Lesions**

D. L. BECKER, H. B. BURCHELL, and J. E. EDWARDS. *Circulation [Circulation]* **3**, 230-238, Feb., 1951. 6 figs., 3 refs.

The pulmonary vascular changes are reported in 2 cases in which the posterior mitral-valve cusp was not functioning. In one this was due to adherence of the posterior mitral-valve cusp to the adjacent ventricular wall in a treated and healed case of subacute bacterial endocarditis; in the other the chordae tendineae of the posterior mitral cusp were ruptured, though the cause could not be determined. The pulmonary arteries showed a variety of pathological changes, such as medial muscular hypertrophy, atheroma, and subintimal occlusive cellular proliferation or fibrosis. These changes had previously been described by other workers as occurring in mitral stenosis. The authors [rightly] point out that the finding of such lesions in mitral insufficiency is important in that it is desirable to avoid, if possible, the production of mitral incompetence in surgical attempts to alleviate mitral stenosis.

G. J. Cunningham

**558. Endophlebohypertrophy and Phlebosclerosis. I. The Popliteal Vein**

M. LEV and O. SAPHIR. *Archives of Pathology [Arch. Path.]* **51**, 154-178, Feb., 1951. 16 figs., 34 refs.

The authors, working at the Michael Reese Hospital and the University of Illinois College of Medicine, Chicago, have studied the structural changes which occur in large veins. The results of the first part of this work deal with changes in the popliteal vein. In advancing age the gross structure of the popliteal vein shows striking changes. The vein becomes thicker and the coarse and fine linear striations in its wall become accentuated. Shortly after birth linear streaks or thickenings appear at the mouths of tributaries, and by the age of 2 years a linear thickening can be seen in that part of the vein which is just to one side of its point of maximal contact with the popliteal artery. After the age of 20 years the thickening becomes more marked and yellow dots and streaks appear; the vessels become firmer to the touch and may feel cartilaginous. The lesions are mostly seen in the condylar and supracondylar portions of the vein, although they may extend throughout its entire length.

The microscopic structure of the vein begins to change soon after birth. On the linear side of the internal elastic lamella there is found a focal proliferation of elastic muscle and collagen fibres. This process is named endophlebohypertrophy; it increases up to 2 or 3 years of age so that at the point of greatest involvement the thickness of the intima may equal that of the media. After 3 years of age there is apparently a diminution in the amount of endophlebohypertrophy. The reason for this is unknown, but it may be related to the assumption of the erect posture. Between the ages of 10 and 20 endophlebohypertrophy has again increased. It has a characteristic layering effect; an outer layer of hypertrophy is superimposed on an inner, separated

by the internal elastic lamella. By this time it can be shown that there is an alteration in the ground substance in the affected regions. In older subjects the endophlebohypertrophy becomes more marked; there is a decrease in the smooth muscle fibres and a great increase in the amount of intimal connective tissue. In the sixth decade areas of vacuolation appear in the plaques. There is a marked loss of elastic fibres, hyalinization in connective tissue occurs and calcification begins. Comparison of cases with and without systemic evidence of right ventricular failure revealed no appreciable difference between the veins in the 2 groups.

The authors discuss the meaning of these changes. They consider that while the process of endophlebohypertrophy is a normal reaction in the vein to mechanical stress, the condition may be abnormally advanced in a young person and thus become a pathological finding. In advancing age senile phlebosclerosis may occur, and this is unrelated to endophlebohypertrophy. It becomes obvious in the fifth decade and is progressive thereafter. It is associated with the loss of muscle fibres in the media and the focal deposition of calcium about the elastic lamella.

A. G. Riddell

**559. Dilatation of the Ascending Aorta with "Gigantism" of the Aortic Valve. (Dilatation du segment initial de l'aorte. Gigantisme de l'appareil valvulaire aortique)**

A. TOURNIAIRE, F. DEYRIEUX, and P. BASTIEN. *Archives des Maladies du Cœur et des Vaisseaux* [Arch. Mal. Cœur] 44, 153-157, Feb., 1951. 3 figs., 4 refs.

A man aged 26 complained of pain on exertion, of recent onset; he had a number of congenital stigmata, such as arachnodactyly, high arched palate, facial asymmetry, thoracic deformity, and kyphosis. There was a loud diastolic murmur with thrill to the right of the sternum, and a quieter systolic murmur was heard best between the scapulae. The femoral pulses were both palpable: blood pressure 140/20 mm. Hg. Radiologically, there was dilatation of the proximal aorta with increased pulsation. The Wassermann reaction was negative. The patient deteriorated and died of congestive failure within a few months.

Necropsy showed left ventricular hypertrophy and a pyriform dilatation of the ascending aorta, with a maximum circumference of 18 cm. just above the aortic valve and a circumference of only 7 cm. at the origin of the innominate artery. The ductus arteriosus was patent.

The aortic valves were normally formed but very large, though competent; the cusps were not adherent, but microscopically were thickened and sclerotic with some calcification. The coronary arteries arose 1 cm. above the attachment of the cusps and were normal. The aortic intima was normal apart from a strip in which it was torn and folded; histologically, there was thickening of the elastic and muscular elements of the aortic wall. There were no chronic inflammatory changes, and the general appearance was quite unlike that of syphilis. The condition was considered to be undoubtedly congenital in origin.

J. A. Cosh

**560. The Sympathetic Ganglions of Hypertensive Patients**

R. C. TRUEX. *Archives of Pathology* [Arch. Path.] 51, 186-191, Feb., 1951. 3 figs., 13 refs.

Contradictory statements regarding the presence or absence of specific lesions in the sympathetic ganglia in certain diseases seemed to warrant further investigation. The present study was made to see if any consistent changes were present in cases of hypertension.

A total of 44 thoracic and lumbar ganglia were removed from 17 persons suffering from arterial hypertension: 21 control ganglia were examined from 18 necropsies within from 1 to 6 hours of death. Cellular changes were observed in both series. Extensive cellular chromatolysis and hyperchromatism of nuclei occurred frequently, which would suggest that there is great variation in the amount of cytoplasmic chromatin in the normal cell and that cytoplasm is readily replenished from the nucleus of the cell itself. These phenomena cannot be regarded as pathological. Neurones with eccentric and multiple nuclei occurred in both series. Particular attention was paid to the capsular and interstitial nuclei. Frequently these nuclei are so numerous and tightly packed as to make it difficult to distinguish capsular, neurolemmal, and interstitial nuclei. Such proliferation, though seen most frequently in carcinomatous persons, is not pathognomonic of any condition. The ganglionic arterioles were examined and there did not seem to be any greater amount of change in the hypertensive series than in the controls. The author points out that while neuronal chromatolysis has proved a valuable method for demonstrating cell effects in disease and experimental lesions, its appearance can be reproduced by prolonged decolorization during the process of preparing slides when certain Nissl methods are used.

J. G. Jamieson

**561. Variants of the Platelet Thrombosis Syndrome and their Relationship to Disseminated Lupus**

P. M. BEIGELMAN. *Archives of Pathology* [Arch. Path.] 51, 213-223, Feb., 1951. 4 figs., 8 refs.

A description of 2 cases is given in which not only were features of platelet thrombosis found, but other conditions were encountered, thus raising the question whether platelet thrombosis could be related to allergic conditions in general and lupus erythematosus in particular. The first patient was a woman, first seen in 1937, aged 43, who was under continuous observation for various complaints, including arthritis, swelling of the legs, precordial pain, palpitation, dyspnoea, dizziness, malaise, vaginal discharge, folliculitis of the buttocks, and occasionally furunculosis. She also developed erythematous nodules on the legs, xanthoma simplex multiplex on knees and buttocks, and crops of macules and papules. Her previous history included syphilis at 33, treated intermittently for 7 years, which had been finally cured. She died in 1947 with a terminal condition (characterized by fever, weakness, anaemia, thrombocytopenia, and sudden death) characteristic of the platelet-thrombosis syndrome. Necropsy revealed platelet

thrombosis of the heart, miliary infarcts of the heart, splenomegaly with thrombosis and infarction, glomerulitis, myositis, and healed polyserositis. The usual icterus had never appeared, but an abnormal albumin-globulin ratio and the results of the thymol turbidity test suggested damaged liver function. The author suggests that the vague symptoms present for 10 years may have been caused by the smouldering disease process, spectacular only in its end stage.

The second patient, a man aged 60, had 2 years' history of fever, chills, and burning precordial pains and recent right-sided lumbar pain and weakness. He had a large liver and spleen. The diagnosis of platelet-thrombosis syndrome was suggested by the history and was confirmed by skin biopsy in 1948, but the mildness of the anaemia and the 2-year history seemed unusual. Later a microscopic sediment in the urine suggested periarteritis or lupus erythematosus. Necropsy in 1949 showed a verrucous endocarditis and glomerular sclerosis suggesting a lupus-erythematosus-like condition. There is some similarity between these 2 cases and those described by Page (*Amer. J. med. Sci.*, 1949, **218**, 425). One might postulate a similar basis for the collagen diseases and platelet thrombosis. A reaction in the intima would give the platelet thrombosis. A general fulminating reaction would result in the rapidly fatal syndrome described by Baehr (*Trans. Ass. Amer. Phys.*, 1936, **51**, 43). A reaction in the vessel wall would give rise to periarteritis nodosa, and reaction in the perivascular mesenchyme would produce a lupus erythematosus type of disease.

J. G. Jamieson

**562. Endocardial Fibroelastosis. Report of Two Cases**  
F. C. COLLIER and P. D. ROSAHN. *Pediatrics* [*Pediatrics*] **7**, 175-181, Feb., 1951. 4 figs., 18 refs.

Endocardial elastic thickening was noted in only 2 among 205 necropsies on children: a reference is made to 11 previous cases. No patient lived more than 5 years and the majority died in less than 1 year; 7 cases were associated with other congenital abnormalities of the cardiovascular system. The aetiology is unknown. A history of maternal infection was obtained in 5 cases. There was no information concerning blood groups.

D. M. Pryce

**563. The Morbid Anatomy of Talc Pneumoconiosis.**  
(Zur pathologischen Anatomie der Talkstaublunge)  
W. DI BLASI. *Virchows Archiv für Pathologische Anatomie und Physiologie* [*Virchows Arch.*] **319**, 505-525, 1951. 9 figs., 15 refs.

The author records the necropsy findings in a man of 54 years who had worked for 17 years in an accumulator factory where he had been constantly exposed to talc dust, which was used to powder moulds when pouring lead plates. He had to give up this employment on account of increasing general weakness and pulmonary complaints, haemoptysis, dyspnoea, and pain in his chest. Radiologically, numerous small lung opacities were demonstrable; these formed larger, confluent masses in both middle and lower zones. The immediate cause of death was bronchopneumonia.

The necropsy was performed 5 weeks after death, but the organs were well preserved. Large pneumoconiotic nodules of a slate colour, measuring up to 8.5 cm. in diameter, were present in both lower lobes and in the lower halves of both upper lobes. They were firm in consistency, although less firm than in silicosis, and frequently somewhat elastic. All other lung areas contained numerous nodules of small or medium size, as well as fibrous strands. A small tuberculous cavity was present in the anterior part of the left lower lobe. There were widespread, broad, fibrous pleural adhesions and both lungs were emphysematous at the apices and along the margins of the lobes. The heart showed hypertrophy and dilatation of the right side. All internal organs were congested and there was some pulmonary oedema. Microscopically, the nodules appeared as greyish or greyish-red, structureless material, often associated with fibrous tissue which showed a tendency towards hyaline degeneration. With special stains this greyish substance proved to contain exceptionally large numbers of foreign bodies in the shape of needles or platelets in quite irregular distribution. Their average length was about double that of the diameter of an erythrocyte. They were embedded in a fine mesh of reticulum fibres. Some particles were incorporated in macrophages, but practically no dust was present in the fibrous tissue. An occasional asbestos-like body was met with. Very small identical nodules were situated at the junctions of alveolar septa, and perivascularly. The unaffected lung parenchyma displayed chronic emphysema. The hilar lymph nodes consisted almost entirely of masses of macrophages incorporating similar foreign bodies. At their margins, where no dust cells were situated, iron-laden histiocytes were noticeable. [No direct reference is made to examination of the dust particles in polarized light.] By chemical, mineralogical, and radiological methods the dust was shown to consist mainly of talc ( $Mg_6(Si_2O_5)_4(OH)_4$ ): quartz was absent. The picture was thus one of a diffuse and nodular talc pneumoconiosis.

The author draws attention to the contrast between these changes and talc granulomatosis due to contamination of tissues during operations. The difference is attributed to the size of the particles, which are fairly large in the case of powder on surgical gloves, whereas only the finest dust penetrates into the lung alveoli.

R. Salm

**564. Two Cases of Giant-cell Granuloma of the Pituitary Gland**  
I. DONIACH and E. A. WRIGHT. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **63**, 69-79, Jan., 1951. 14 figs., 7 refs.

A description is given of 2 cases of giant-celled granulomatosis of the pituitary gland, with disseminated granulomatous lesions in other organs. The first patient was a woman of 43 who had a non-toxic goitre from the age of 30. At 38 her periods ceased abruptly, followed by asthenia, shakiness, headaches, and loss of weight; these symptoms continued for 5 years. Death occurred suddenly after a short period of coma. At necropsy the pituitary was normal in size, the thyroid

was nodular, while the adrenals, uterus, and ovaries were atrophic. An early haemorrhagic bronchopneumonia was demonstrable and a single miliary tubercle was discovered in the spleen. Histologically, 80 to 90% of the substance of the anterior pituitary was occupied by granulomatous tissue consisting of degenerated pituitary cells, macrophages, neutrophils, eosinophils, lymphocytes, plasma cells, and multinucleated giant cells with one, or occasionally two, rings of nuclei incorporating flaky, haematoxyphilic, birefractile material. These cells were supported by a dense reticular mesh. Follicular masses of epithelioid-like cells, with or without giant cells, were contained in the capsule of the organ, while a few paravascular collections of macrophages associated with a giant cell were present in the posterior part. The adrenal cortex showed marked atrophy, but the entire medulla was replaced by macrophages, giant-cells, and lymphocytes; an occasional follicular arrangement was discernible. The ovary contained unripe follicles. No tubercle bacilli were demonstrable in sections from pituitary and adrenals.

The second case was that of a man of 60 years who died of sudden heart failure after a 9 months' history of cardiac complaints. He had never shown signs of pituitary disease. At necropsy there was generalized arteriosclerosis and congestion of the internal organs. The heart was hypertrophied, but the pituitary appeared macroscopically normal. Histologically, however, the latter organ showed a condition similar to that of the first case, granulomatous tissue occupying about 70% of the pars anterior. In addition, an arteriole in the pituitary stalk was surrounded by a circular band of identical granulation tissue, composed chiefly of macrophages and some lymphocytes. The lumen of both coronary arteries was occluded by recent and older blood clot, while the media was found to be replaced by a band of granulation tissue similar to that in the pituitary; this tissue was spreading into the adjacent adventitial fat. A modest degree of round-cell infiltration, with an occasional giant cell, was present in the portal spaces of the liver. The authors were unable to decide whether the condition in these cases was of specific origin (syphilis, tuberculosis, sarcoidosis), or whether it was due to a primary parenchymatous necrosis of the anterior part of the pituitary.

R. Salm

#### 565. A Contribution to the Pathology of Sjögren's Disease

P. ELLMAN, F. P. WEBER, and T. E. W. GOODIER. *Quarterly Journal of Medicine* [Quart. J. Med.] 20, 33-42, Jan., 1951. 7 figs., 7 refs.

A case of Sjögren's disease is described lasting 8 years, beginning in a woman of 35, with dryness of the mouth and painless parotid swellings and ending with bronchopneumonia following a spontaneous pneumothorax. At necropsy, chronic inflammatory changes with degeneration and atrophy were found in the lacrimal, salivary, and mucus-secreting glands of the nasopharynx and respiratory and upper alimentary tracts, and in sweat glands of the skin. It is suggested that this

inflammatory atrophy, of unknown causation, forms the pathological basis of the disease and that the resulting dryness leads to obstruction of the ducts, resulting in a secondary inflammatory granulomatous process and possibly suppuration.

[Professor Dorothy Russell's detailed description of the histological appearances in 36 slides gives additional value to this report.]

Ernest T. Ruston

#### 566. My Conception of Cellular Nevi

P. MASSON. *Cancer* [Cancer] 4, 9-38, Jan., 1951. 25 figs., 17 refs.

This outline of the neurogenic hypothesis of the origin of pigmented naevi by its originator is clear and timely. The origin of naevi is said to be twofold, from epidermal melanoblasts which multiply and spread into the dermis, and from the Schwann cells of the cutaneous nerves which multiply and infiltrate the deeper dermis. These two components merge and become indistinguishable from each other. The epidermal melanoblasts are specific cells, distinct from the rest of the epidermal cells; their precise source developmentally is still debatable, possibly from the neural crest, possibly from the epidermis itself. In a pigmented naevus which has become malignant it is very difficult to determine histologically whether both of the two components of the naevus may have been the source of the growth. While there is no doubt that malignant change often involves the epidermal melanoblasts, two specimens lead the author to believe that the "neuroid" elements could have been the source of the growths.

R. A. Willis

#### 567. Aberrant Pyloric Glands in Regional Ileitis

A. F. LIBER. *Archives of Pathology* [Arch. Path.] 51, 205-212, Feb., 1951. 4 figs., 11 refs.

In 4 of 5 cases of regional ileitis the affected areas of ileum contained glands of pyloric type, widely scattered. Each tube lined by pyloric epithelium was continuous with and deep to the Paneth cell segment at the base of a Lieberkühn crypt. The wide distribution of the aberrant pyloric glands excludes their origin from Meckel's diverticulum or other heterotopic tissues.

It is suggested that the pyloric glands are newly formed and that the mucus secreted by them may compensate in part for that lost by the destruction of normal muciparous glands in regional ileitis.—[Author's summary.]

#### 568. Fibrous Dysplasia of Bone. (Displasia fibrosa de los huesos)

H. VALLS and F. SCHAJOWICZ. *Revista de Ortopedia y Traumatología* [Rev. Ortop. Traum.] 20, 83-119, Oct., 1950. 33 figs., bibliography.

In this careful study of 26 cases of monostotic and polyostotic fibrous dysplasia of bone the authors have found no support for Thannhauser's theory (1944) that such dysplasia is closely related to neurofibromatosis. Many fine photomicrographs are reproduced of the structural elements of the lesions, among which are

no nervous elements similar to those seen in neurofibroma. There is a survey [rather incomplete] of the literature, followed by a description of the method of investigation and a somewhat detailed survey of the cases with illustrations of x-ray and pathological findings.

[It is a pity that so much painstaking work is still wasted on attempts to prove or disprove theories concerning pathogenesis with the aid of histological methods. The abstracter (*Ergebn. Chir. Orthop.*, 1933, **26**, 328) took this view in a detailed study of osteitis fibrosa, restated in more general terms in the *Lancet* (1939, **1**, 186).]

L. Michaelis

**569. The Morbid Histology of the Muscles in Rheumatoid Arthritis.** (Sull'istopatologia dei muscoli nella poliartrite cronica primaria)

T. GALLI and F. MORIN. *Revue de Rhumatisme [Rev. Rhum.]* **18**, 59-73, Feb., 1951. 7 figs., 21 refs.

The authors give an excellent review of previous work in this field and detail the various views held as to the pathogenesis of the nodules which occur in rheumatic conditions. They have studied 11 cases of rheumatoid arthritis, performing muscle biopsies in all. The technique used is described, and clinical details and histological findings (with photomicrographs) are given in each case. The findings were similar in all cases and are in agreement with those of other workers, although more importance is attached to the changes in the muscle fibres. The small-celled infiltrations in the connective tissue are considered to be similar to those found in other "collagen diseases", whether in many tissues as in disseminated lupus erythematosus and diffuse scleroderma, or localized as in thromboangiitis obliterans or periarteritis nodosa. The lesions in the muscle fibres consist in changes in the number of nuclei, varying from a very slight increase to a great increase, with nuclei forming masses. The various grades of change are thought to be purely quantitative. It had been hoped to prove that muscle biopsies are as useful a diagnostic aid in rheumatoid arthritis as sternal puncture is in haematology, but the conclusion is reached that the changes found are not specific, but are due to muscular atrophy and can be found in other conditions causing such atrophy.

R. F. Jennison

**570. The Myopathy of Mongolism. A Histological Study.** (La miopatia del mongolismo. Studio istologico)

L. PERALE. *Clinica Pediatrica [Clin. pediat., Bologna]* **32**, 663-684, Dec., 1950. 7 figs., 1 ref.

The author of this paper, which comes from the Department of Human Anatomy, University of Padua, and the Pediatric Hospital, Venice, reports his histological researches on striated muscle in male mongols. A preliminary note on the subject has already been published (*Att. Soc. med.-chir., Padova*, 1948, **26**, 30). A number of cases of mongolism were studied and biopsy performed on the gluteal muscles and the quadriceps, while, for purposes of control, studies were carried out on homologous muscles from normal boys. There

were 14 cases of mongolism, their ages varying from 20 days to 5 years, the controls ranging from 30 days to 3 years. The histological technique used consisted in elastin staining by Hollbornn's method and with haematoxylin-eosin. Muscles obtained from mongols showed Zenker's degeneration of the muscle fibres in 71.4% of cases. The number of muscle fibres which were affected varied in different parts of the muscle and the degeneration was not uniform in its distribution, although it could be found in certain zones. Another change, which was not found so frequently but was present in 4 cases, was fragmentation of the muscle fibres. The stroma showed proliferation of the elastic fibres, especially in connexion with the degeneration. According to the author it is difficult to establish whether the histological findings are in proportion to the clinical signs, especially the muscular hypotonia. The impression is that there is a correlation between the more marked clinical signs and the more extensive histological findings. No relation was noted between the muscular findings and the factors which are usually regarded as important in the aetiology of mongolism. In these cases there was no history of numerous pregnancies on the part of the mother, no advanced age of the parents, and neither tuberculosis nor syphilis were present. The histological changes in the muscle fibres are regarded as congenital, and the proliferation of the collagenous and elastin stroma as secondary to these changes. From the histological point of view there is a real myopathy in mongolism.

E. Forrai

**571. Glycogen Storage Disease. I. Familial Cardiac Glycogen Storage Disease: Report of Two Cases and Discussion of Relation to Other Forms of Abnormal Glycogen Deposition**

B. H. LANDING and R. BANGLE. *Bulletin of the International Association of Medical Museums [Bull. int. Ass. med. Mus.]* **31**, 84-109, Nov., 1950. 10 figs., bibliography.

The clinical features and necropsy and histological findings are described in 2 cases of cardiac glycogen-storage disease occurring in brothers who died aged 43 months and 2½ months respectively. Necropsy was performed 5 and 8 hours after death respectively and the chief finding was gross cardiac enlargement. The heart weights were 67 g. (normal 27 g.) and 88.5 g. (normal 23 g.). The ductus arteriosus was closed and there was a patent, slit-like foramen ovale in both cases. Histologically, the heart muscle fibres contained large central "vacuoles" surrounded by a fringe of myofibrils. The "vacuoles" failed to take fat stains, but were coloured by Best's carmine and periodic acid-leuko-fuchsin stains.

On searching the literature the authors found 35 cases of the disease reported, of which 31 are summarized in tabular form. The condition appears to occur in two well-defined age groups, namely, in infancy and during adolescence and, like many other metabolic disorders, is more severe and rapidly progressive in the younger patient. From the literature available the authors conclude that cardiac glycogen-storage disease differs

from the hepatic form in that the former may be a sex-linked condition, whereas the latter probably is not. The available evidence is inconclusive as to whether the disease is inherited as a Mendelian dominant or recessive character. No case embodying both cardiac and hepatic glycogen storage has so far been described.

Single and multiple rhabdomyomatosis is probably commoner than cardiac glycogen-storage disease, the histology of the two diseases is different, and the former condition tends to be associated with tuberous sclerosis.

"Diffuse cardiac rhabdomyomatosis" in all probability does not exist as a definite disease entity.

R. B. T. Baldwin

**572. Glycogen Storage Disease. II. Histochemical Studies of Glycogenolysis in Human Hearts Obtained Postmortem, with Special Reference to Glycogen Storage Diseases**

R. BANGLE. *Bulletin of the International Association of Medical Museums* [Bull. int. Ass. med. Mus.] 31, 110-123, Nov., 1950. 18 refs.

Histochemical detection of glycogen in sections of human heart tissue was carried out as follows. The usual technique for paraffin sections was employed, but absolute alcohol and alcohol-formalin (1 part formalin and 9 parts 95% alcohol) were used as fixatives. After removal of paraffin wax the sections were washed in distilled water for 5 minutes, after which they were placed in 0.3% nitric acid containing 0.8% potassium metaperiodate for 10 minutes, and then were washed in running tap-water for 5 minutes. They were placed in Schiff's leukofuchsin reagent for 15 minutes and rinsed in M/20 sodium bisulphite solution three times, each time for 90 seconds. Finally the sections were rinsed in running tap-water and mounted in the usual manner after counterstaining. All sections were controlled by diastase digestion preparations, the same procedure as above being followed except that before staining the sections were incubated for one hour at 37° C. in freshly prepared 0.1% malt diastase buffered at pH 6.0. Quantitative estimations were done on small pieces of heart kept at -4° C. or in absolute alcohol. Normal infant hearts contained 0.14 to 0.18 g. of glycogen per 100 g. fresh weight, but this amount could not be demonstrated histochemically.

Glycogen appeared as bright red or purple granules; sometimes as a bright red blotching of the heart muscle. Glycogen was found in 61% of adult hearts and 75% of infant hearts, no matter from what part of the heart the section was taken. In all, 113 hearts were examined. There was no correlation between the glycogen content and age, sex, time of necropsy after death, or size of heart. Accumulation of glycogen is not necessarily accompanied by hypertrophy, but in cardiac glycogen-storage disease hypertrophy is pronounced and is diffuse.

In glycogen-storage disease the glycogen is unusually stable after death, and whereas heart mash from a case of cardiac glycogen-storage disease is unable to produce glycogenolysis in hearts from persons suffering from glycogen-storage disease, diabetes, or non-diabetic disease, heart mash from a normal heart is capable of so

doing, even when phloridzin, which inhibits phosphorylation, is added.

[From these and other experiments it would appear that there is in the blood of normal persons an unusually stable glycogenolytic enzyme, not inhibited by phloridzin but partially inhibited by temperatures of 5° C. The author suggests that this enzyme is probably blood diastase. Thus it is suggestive that there is a greatly diminished or absent blood diastatic activity in persons with glycogen-storage disease. On the other hand, unless glycogenesis in these cases involves some substrate other than glucose, the question occurs why, if in glycogen-storage disease glycogenesis can take place (as obviously it must), the tissues from these cases are incapable of bringing about the reverse reaction, since the two processes are caused by similar enzyme systems? Clearly the matter requires further investigation. Those who are interested in this problem should refer to the original paper.]

R. B. T. Baldwin

CLINICAL PATHOLOGY

**573. Determination of Haemoglobin. VIII. Accuracy of Methods Applied to Abnormal Bloods**

E. J. KING, R. J. BARTHOLOMEW, M. GEISER, S. VENTURA, I. D. P. WOOTTON, R. G. MACFARLANE, R. DONALDSON, and R. B. SISSON. *Lancet* [Lancet] 1, 1044-1045, May 12, 1951. 12 refs.

**574. Renal Excretion of Bile Pigments. (L'excrétion des pigments biliaires par les reins)**

H. DEENSTRA. *Annales de Médecine* [Ann. Méd.] 51, 685-700, 1950. 23 refs.

The author has studied the renal excretion of bilirubin in 11 cases of hepatitis, in 3 cases of obstructive jaundice, 2 of which were due to stone and one to carcinoma of the pancreas, and in 1 case of jaundice recurring after cholecystectomy. Large quantities of bilirubin were found in the urine in the obstructive conditions, in severe hepatitis, and during the early stages of cases of prolonged hepatitis. A very small urinary excretion of bilirubin was observed in a patient with mild jaundice dying after 7 days with signs of acute liver insufficiency. The speed of the direct diazo reaction for bilirubin in the blood was found to bear no relation to the extent of urinary excretion of the pigment. The renal threshold for bilirubin, defined by the author as lying between the last serum bilirubin concentration (mg. per 100 ml. serum) measured before bilirubin disappeared from the urine and the first serum bilirubin concentration determined after the bilirubin disappeared from the urine, was measured in each case. When the icterus was diminishing regularly the value for the threshold was obtained by interpolation. The author found a wide range of values for the renal threshold or "direct" reacting bilirubin, and could detect no bilirubin in the urine in a case in which a serum concentration of 22 mg. per 100 ml. of "indirect" reacting bilirubin was obtained.

[A much larger series of observations on the renal threshold of bilirubin has been reported by Vickers

(*J. clin. Path.*, 1950, 3, 271), who found that there was no one renal threshold for bilirubin. A modal level of between 0.8 and 1.0 mg. per 100 ml. was observed in a minority of cases of "direct" bilirubinaemia, but much higher levels occurred in "indirect" bilirubinaemia. One of the difficulties in the investigation of the renal threshold for bilirubin is the lack of sufficiently sensitive tests for the pigment in urine, and the technique proposed by Ingham (*Lancet*, 1951, 1, 151) may be of value in this connexion.]

M. J. H. Smith

**575. Comparison of Excretion of Bromsulphthalein and Sodium Cholate after Intravenous Injection, Separately and Combined**

H. W. BAKER, C. E. ANDERSON, and R. H. MCCLUER. *Proceedings of the Society for Experimental Biology and Medicine* [Proc. Soc. exp. Biol., N.Y.] 76, 216-220, Feb., 1951. 2 figs., 20 refs.

Cholic acid and glycocholic acid were estimated in serum by the following fluorophotometric method. To 8.5 ml. of 95% alcohol was added 0.5 ml. of a solution containing 5% w/w barium oxide and 0.4% w/w barium acetate. After the addition of 1.0 ml. of serum the mixture was boiled for 2 minutes, cooled, and alcohol added to 10 ml. After filtration, 3.0 ml. of the filtrate was transferred to a centrifuge tube and evaporated to dryness under reduced pressure at 40 to 45° C.; 4.0 ml. of ethyl acetate followed by 0.1 ml. of 3.3% w/w solution of calcium oxide in the same solvent was added and the mixture heated for 2 minutes at 90° C., centrifuged, and the solvent decanted. This last stage, except for the addition of the calcium oxide solution, was repeated twice: 10.1 ml. of a mixture consisting of 9 parts of concentrated sulphuric acid and 1 part of glacial acetic acid was then added to the residue, which was heated for 30 minutes in a waterbath at 37° to 40° C. The fluorescence was then measured in a fluorophotometer, the reading of the sample being compared to a standard curve prepared from a graded series of solutions of cholic acid in the acetic-sulphuric acid mixture. The method was found to be unreliable for bile acids containing less than three hydroxyl groups.

Bromsulphalein (BSP) and cholic acid tolerance tests were performed on dogs in health and following liver damage induced by carbon tetrachloride. Liver biopsies of the latter group on histological examination showed central coagulation necrosis. The cholic acid solution, which was injected intravenously, contained 50 mg. of cholic acid per ml. in 25% glucose and was adjusted to pH 7.4 with sodium hydroxide. A dose of 50 mg. of cholic acid per kg. body weight was given. In each dog BSP and cholic acid tolerance tests were performed independently and simultaneously.

The results showed that when a mixture of BSP and cholic acid was injected in healthy dogs the concentration of BSP in the serum was greatly increased 5 and 15 minutes after administration, whereas the cholic acid concentration was normal. In the dogs with liver damage the BSP excretion was significantly retarded, but the cholic acid excretion only slightly delayed, when these tests were performed independently. When a mixture

of the two substances was injected the BSP retention paralleled roughly that observed in the independent test, but was 35 to 60% higher, and the cholic acid retention was only slightly increased. The authors consider that the BSP test may be rendered more sensitive by simultaneously giving cholic acid. M. J. H. Smith

**576. The Coprological Diagnosis of Steatorrhœa. (Recherches sur le diagnostic coprologique des stéatorrhées)**

R. GOIFFON and F. NEPVEUX. *Archives des Maladies de l'Appareil Digestif* [Arch. Mal. Appar. dig.] 39, 1267-1277, Dec., 1950. 2 figs., 32 refs.

The authors give an account of the steatorrhœas and the various fatty acids and soaps occurring in the faeces in this group of diseases. They describe two relatively quick methods of alcohol and ether extraction of the fatty contents of the faeces and compare these methods with their own technique, which utilizes the fact that the fatty acids are soluble to different degrees in acetone heated to varying temperatures. The technique is as follows: 5 ml. of a 10% aqueous solution of faeces, 10 ml. of acetone, and 10 drops of 10% hydrochloric acid are placed in an Erlenmeyer flask and brought to the boil. When on the point of boiling, 5 to 6 ml. is rapidly filtered through a funnel heated to 40° C. into a tube (I). The remaining mixture in the flask is cooled under running water and left at room temperature for 30 minutes, after which time it is also filtered into a tube (II); 5 ml. of each filtrate is mixed with 10 ml. of N/20 hydrochloric acid and left for 30 minutes. At the end of this time the two filtrates are examined photometrically with red light and their translucency is measured in Verne degrees. Tube I contains stearic, palmitic, and oleic acids, and Tube II contains oleic acid only. The neutral and unsaponifiable fats do not pass into the filtrates.

From the optical densities of the filtrates the weights of fatty acids present can be calculated from a table equating known weight/volume values of fatty acids against the corresponding optical densities. The upper limit of normal is 3.5 g., which corresponds to an optical density of 60 Verne degrees.

A short description is also given of polarimetric examination of faeces. Faeces are mixed with hydrochloric acid, heated to 50° C., and rapidly cooled. On cooling, luminous crystals appear—quickly if there is an excess of free fatty acids, and more slowly if there is a relative excess of oleates. The suspension of crystals is then examined in the polarimeter. The authors stress that these methods must of course be combined with the usual microscopical examination of faeces to investigate the presence of undigested food and other abnormal features.

René Méndez

**577. Electrophoretic Serum Protein Fractions in Hepatobiliary Disease**

H. POPPER, W. B. BEAN, J. DE LA HUERGA, M. FRANKLIN, Y. TSUMAGARI, J. I. ROUTH, and F. STEIGMANN. *Gastroenterology* [Gastroenterology] 17, 138-162, Feb., 1951. 11 figs., bibliography.

# Microbiology

## VIRUSES

578. **Studies on Chemotherapy of Vaccinia Virus. I. An Experimental Design for Testing Antiviral Agents**  
K. A. BROWNE and D. HAMRE. *Journal of Bacteriology* [J. Bact.] **61**, 127-134, March, 1951. 5 refs.

When testing the effect of a chemotherapeutic substance on a virus by comparing the LD<sub>50</sub> for treated and untreated chick embryos, the sensitivity of the test is increased by estimating survival time in relation to the dilution of the viral inoculum. The vaccinia virus used in these experiments was a rich chorio-allantois culture that had been stored in the frozen state at -70° C. This was thawed out and diluted in nutrient broth to provide approximately 360, 180, and 90 LD<sub>50</sub> doses respectively in 0.25 ml. Each dose was injected into a group of six 6-day-old chick embryos for each substance to be tested and into a group of six which were to be treated with normal saline as controls. Each substance was tested, therefore, in 18 eggs (3 groups of 6 eggs each). The substance to be tested was injected in 0.5-ml. amounts into the yolk sac 30 minutes after infection with the virus. The eggs were incubated at 36° C. and candled twice daily. The membranes of the dead eggs were examined for pocks to confirm the cause of death. All materials injected into the eggs were tested beforehand for sterility.

The authors' hypothesis was that a given concentration of an active compound reduced the virus concentration by a constant fraction independent, over a fair range, of the concentration of the virus.

The activity of the compound was calculated from mean survival times over a small range of virus dilutions. This was checked against a standard curve prepared from results of tests with a wider range of dilutions and further checked by employing a larger number of eggs with a single dilution of virus and a particular concentration of the compound and finding out from the actual mean reciprocal survival time, through the standard curve, what the calculated virus dilution should have been to give such a survival time.

The paper gives results obtained with *p*-aminobenzaldehyde and 3-thiosemicarbazone. The agreement of the direct and indirect methods is in favour of the authors' hypothesis.

H. J. Bensted

579. **The Interaction of Virus and Cell Surface**  
F. M. BURNET. *Proceedings of the Royal Society. B. [Proc. roy. Soc. B.]* **138**, 47-64, Feb. 15, 1951. 1 fig., 23 refs.

This paper, which was read before the Royal Society as the Croonian Lecture for 1950, summarizes the work of the author and his colleagues on the interaction between virus and host cell. [Much of this work has already been published and reviewed in these *Abstracts*.]

It is an extraordinarily stimulating summary of a vast body of work, but is much too long and detailed for adequate abstraction.] Suffice it to say that all the evidence is marshalled in favour of the view that the particles of pathogenic viruses (in this case influenza and related viruses) can enter the host cell because "embedded in the cell surface and intimately related to the other components are mucopolysaccharide macromolecules, composed of a number of subunits" to which the virus particles can attach themselves. They are then released into the cell because the receptors are "susceptible to attack by the enzyme common to the receptor-destroying enzyme (of *Vibrio cholerae*) and the viruses of this group".

The remainder of the paper consists for the most part of a discussion of the implications of this hypothesis, but in conclusion the author reviews recent work on the multiplication of the virus in the cell after its entry. This is not, as was at one time supposed, merely simple binary fission such as occurs in bacteria, but something much more complicated and elaborate. This prompts the question with which the paper ends:

"What are the processes by which energy and building stones are utilized in the replication of organic pattern within living organisms? And I would hope that the first approach toward an answer to that question might come from the study of intracellular virus activity that is beginning at the present time."

R. Hare

580. **Interference Effects in Infectious Diseases. (Über Interferenzerscheinungen bei Infektionskrankheiten)**  
O. VIVELL. *Ergebnisse der Inneren Medizin und Kinderheilkunde [Ergebn. inn. Med. Kinderheilk.]* **2**, 680-712, 1951. Bibliography.

[This detailed review of interference phenomena in relation especially to virus diseases, from the Universitätskinderklinik, Freiburg i. Br., Germany, should be read in the original by all those interested.]

G. M. Findlay

## BACTERIA

581. **Blood Media for the Cultivation of *Mycobacterium tuberculosis***

M. S. TARSHIS and A. W. FRISCH. *American Journal of Clinical Pathology [Amer. J. clin. Path.]* **21**, 101-113, Feb., 1951. 1 fig., 16 refs.

In the experiments described it has been demonstrated that human blood media support the growth of very small inocula of tubercle bacilli. When comparisons with three standard tuberculosis media were made, the blood-containing media proved to be equal to and in many cases superior to the others from the standpoint of early detection and final degree of growth. These

results were based upon experiments not only with a standard laboratory strain of tubercle bacillus (H37 Rv) but also with other virulent human strains isolated directly from sputum under routine diagnostic conditions.

Whenever blood was present in adequate concentrations (15 to 50%), the growth of small inocula of tubercle bacilli regularly occurred. This fact proved to be true regardless of the basal medium used, the presence or absence of glycerine, egg yolk, or a combination of both. Actually most of these substances showed some degree of inhibition of growth when they were incorporated into the blood media, particularly when the concentration of blood was below 15%.

It was also found that fresh defibrinated, citrated, oxalated and even 56-day-old out-dated bank blood were equally effective in supporting the growth from small inocula of tubercle bacilli. Heating the blood, however, resulted in a slight but definite loss in nutritive value.

The blood media herein described should be thoroughly investigated for their diagnostic value. For this purpose either Bordet-Gengou agar or blood agar-base hydrated with 1% glycerine and containing 25% bank blood is recommended. The chief advantages of such media are their economy, simplicity of preparation, and ability to grow tubercle bacilli from small inocula easily, recognizably, and in a short period of time. Both the dehydrated basal media and the out-dated bank blood are readily obtainable and small quantities of fresh media may be quickly prepared. All these factors should encourage a wider use of cultural technics for the isolation of tubercle bacilli. Preliminary experiments indicate that the blood media may be satisfactorily employed for streptomycin sensitivity tests, an important procedure in the field of therapy.—[Authors' summary.]

#### 582. Effective Use of Penicillin to Reduce Contamination in Sputum Concentrates to be Examined for Tubercle Bacilli

J. N. ABBOTT. *American Journal of Public Health [Amer. J. publ. Hlth]* 41, 287-291, March, 1951. 19 refs.

A series of 13,031 specimens of sputum were examined by culture for tubercle bacilli; about 80% of the specimens were from out-patients. Each was homogenized with an equal volume of 4% sodium hydroxide for 15 minutes and centrifuged for 20 minutes at 2,000 r.p.m.; the deposit was then neutralized with hydrochloric acid in the presence of phenol red. Of the 13,031 specimens, 3,544 were inoculated without further treatment into three or four tubes of Löwenstein-Jensen medium, the other 9,744 being further treated with penicillin. A solution of benzyl penicillin (2,000 units per ml. saline) was prepared and added in amounts of 0.1 ml. before inoculation. The final concentration was 100 to 200 units per ml. of deposit.

It was found that the general contamination rate was reduced from 16.5% in the control group to 9% in the penicillin-treated group. The contaminants were isolated and identified in each group and it was found that, while contamination due to streptococci and Gram-positive bacilli was much reduced, the contamination due to

Gram-negative bacilli was about the same in both groups. Other findings were that the number of positive cultures was increased in the penicillin-treated group, but that the early growth was slightly delayed and the final amount of growth was slightly diminished. The action of penicillin was found to last from 3 to 10 days in Löwenstein-Jensen cultures incubated at 37° C.

The author tried the addition of penicillin in amounts of 10 to 125 units per ml. of medium before inactivation; he states that the results were inconclusive. He warns against the addition of penicillin to media containing the wetting agent "tween 80", as this has a very marked bacteriostatic effect on the growth of the tubercle bacillus.

A. G. S. Heathcote

#### 583. Resistance to Streptomycin of Tubercle Bacilli Isolated from Patients Treated with Streptomycin

S. H. FERESEE and F. W. APPEL. *Public Health Reports [Publ. Hlth Rep., Wash.]* 66, 277-288, March 2, 1951. 1 fig., 1 ref.

A series of 157 patients with pulmonary tuberculosis were treated with streptomycin (20 mg. daily in 3 equal doses) for 13 weeks. During the 5th and 9th weeks of this period, and afterwards at 13-week intervals up to 66 weeks after the end of treatment, 24-hour sputum or gastric-lavage samples were cultured, and subcultures in Dubos's liquid medium were used for determining sensitivity to streptomycin. The subcultures were inoculated into streptomycin-free media and media containing 3, 10, or 100 µg. streptomycin per ml. Growth in the last two concentrations indicated moderate and strong resistance respectively.

At the beginning of the test all cultures were positive for non-resistant organisms. At the end, only 55% of cultures were positive, and of these two-thirds showed moderate and strong resistance to streptomycin. Some evidence is given to show that tubercle bacilli from a given patient may show variations in streptomycin resistance after treatment with that drug.

E. A. Brown

#### 584. An Interpretation of Results Obtained from Cultivation of Sputum Samples for *M. tuberculosis*

E. M. MEDLAR, S. BERNSTEIN, and F. C. REEVES. *American Journal of Public Health [Amer. J. publ. Hlth]* 41, 292-301, March, 1951. 7 refs.

Although the growing of *Mycobacterium tuberculosis* from sputum specimens requires good technical procedures for processing specimens, with meticulous attention given to details and a proper culture medium for growing the organism, the interpretation of the results obtained must be considered in relation to the pathologic condition of pulmonary lesions. There frequently is little correlation between the bacillary content of tuberculous lesions and the amount of growth obtained from sputum specimens on the best of culture media. This is due primarily to the irregular distribution of bacilli in necrotic lesions and to the extremely small amount of debris that may be sloughed from such lesions. This disparity between the results of cultures and the bacterial content of necrotic lesions should not be taken to indicate

that no bacilli are being sloughed from such lesions. The unpredictable results obtained from culture of smear-negative sputa or of fasting gastric contents are largely influenced by the status of the pathologic lesion. Because of this situation caution should be exercised in the interpretation of "conversion" of sputum from the results of smear or culture methods.

A comparison of five different media tested in a routine diagnostic service on 2,157 specimens is presented. Each medium tested gave a high percentage of growth of *M. tuberculosis* from smear-positive specimens. Superior results were obtained with the ATS media, slightly modified, in cultures from smear-negative specimens.

The procedures used for growing *M. tuberculosis* in a routine diagnostic service should be geared to the most efficient method for obtaining growth when bacilli are present in small numbers. As simple a procedure as is consistent with efficiency is to be preferred. The results obtained from the technic of preparation of specimens and media and the comparison of the slightly modified ATS medium with other media presented in this paper indicate that the bacteriologic procedures originally adopted in this laboratory in 1947 for growing *M. tuberculosis* are equal, if not superior, to other procedures which have been suggested.—[Authors' summary.]

**585. Metabolism of *Clostridium botulinum*.** (О метаболизме *Bacillus botulinus*)

A. K. RODOPULO. *Микробиология [Mikrobiologiya]* 20, No. 1, 26-32, 1951. 3 refs.

Cultures of *Clostridium botulinum* type A were made in 1-litre flasks in peptone broth, alone and also with the addition of 1 to 2% of glucose. At intervals up to 10 days samples of medium were withdrawn and pH, redox potential, and volatile acid, aldehyde, acetone, alcohol, and toxin content determined by appropriate methods. The amount of gas evolved was determined by weighing the flasks at intervals; it reached a maximum after 40 hours and ceased after 88 hours. The pH fell from 7 to below 6 and the growth of the organisms was consequently inhibited. The redox potential fell from an initial value of -0.006 to -0.265 mV after 160 hours. The concentration of volatile acids in the medium increased during the first few days of growth and then fell after attaining values equivalent to 16 ml. of 0.1 N alkali per 100 ml.; the acids were identified as acetic and butyric and were produced in the proportion of 1:2. Acetone, ethyl alcohol, and butyl alcohol increased in amount throughout the whole period of growth, but the concentration of aldehyde decreased after 15 hours. The gases formed were carbon dioxide and hydrogen, in proportions up to 2.3:1, together with some nitrogen and traces of hydrogen sulphide and mercaptan. The production of toxin increased to reach a maximum at 160 hours, and its concentration then remained at a high level probably as a result of the continual breakdown of bacterial cells. In the absence of glucose, fermentation and gas formation were much reduced and no fall in pH took place; after 40

hours of incubation much of the protein of the medium had been broken down to amino-acids and ammonia. After 112 hours there was a fall in the concentration of amino-acids and a rise in the amount of free ammonia and non-volatile acids. This process continued until 75% of the protein of the medium had been broken down after 10 days of incubation.

D. J. Bauer

**586. *In vitro* Studies of Bacterial Resistance to Chloramphenicol (Chloromycetin)**

G. L. COFFEY, J. L. SCHWAB, and J. EHRLICH. *Journal of Infectious Diseases [J. infect. Dis.]* 87, 142-148, Sept.-Oct., 1950. 1 fig., 7 refs.

Cultures of *Klebsiella pneumoniae*, *Aerobacter aerogenes*, *Salmonella typhi*, *Bacterium coli*, *Bacillus proteus*, *Pseudomonas aeruginosa*, and *Alcaligenes metacaligenes* were transferred 20 times in chloramphenicol-containing broth. Each transfer was made from the tube with the highest concentration of chloramphenicol showing growth into tubes containing higher concentrations of the antibiotic. The resistance of these organisms to chloramphenicol increased gradually. After 20 transfers the resistance of *K. pneumoniae* had increased 10 times, *Ps. aeruginosa* and *S. typhi* 50 times, and *Bact. coli* 125 times. The determination of the increased resistance of the other 3 organisms, which was initially very high, was limited by the solubility of the antibiotic. Upon subsequent transfers in chloramphenicol-free broth the resistance decreased gradually, but did not return to the original levels.

In discussing these results the authors state that the development of resistance to chloramphenicol is more like that encountered with penicillin than with streptomycin. There are two possible explanations for the development of resistance: either the organism may develop a secondary metabolic pathway enabling it to circumvent those enzymatic reactions blocked by the antibiotic, or it may increase the formation of enzymes capable of degrading the antibiotic. The correct explanation remains to be determined.

A. W. H. Foxell

**587. Relation of Penicillin Sensitivity in Staphylococci to Clinical Manifestations of Infection**

J. C. SHERRIS and M. E. FLOREY. *Lancet [Lancet]* 1, 309-312, Feb. 10, 1951. 13 refs.

Recent reports have suggested a general increase in the incidence of penicillin-resistant strains of *Staphylococcus pyogenes*, and the authors feel that this view requires some modification. They bring forward evidence to show that resistant strains are more frequently associated with superficial lesions, but that in acute and closed or deep-seated infections penicillin-sensitive staphylococci are predominant. It is agreed that the high proportion of resistant strains now being reported is due either to a high carrier rate of this type in hospital staffs or to their greater chances of survival in a penicillin-rich environment, but it is emphasized that the high carrier rate is not a reflection of the relative incidence of sensitive and resistant strains in suppurative lesions. Of 35 strains from serious inflammatory conditions 30 were

found to be penicillin-sensitive, and of 53 strains isolated from post-operative infections, pressure sores, and similar superficial lesions, 50 were penicillin-resistant. All the penicillin-sensitive strains studied in these observations had a sensitivity of the same order as the classical Oxford strain, and all the resistant strains were found to produce penicillinase.

H. J. Bensted

**588. Paratyphoid-B Vi-phage Typing**

A. FELIX and B. R. CALLOW. *Lancet [Lancet]* 2, 10-14, July 7, 1951. 13 refs.

**PROTOZOA**

**589. Some Observations on the Variation of Virulence and Response to Chemotherapy of Strains of *Entamoeba histolytica* in Rats**

R. A. NEAL. *Transactions of the Royal Society of Tropical Medicine and Hygiene [Trans. roy. Soc. trop. Med.]* 44, 439-452, Feb., 1951. 1 fig., 26 refs.

A study of the virulence and response to drug treatment of *Entamoeba histolytica* was carried out in young rats (weighing 20 to 30 g.) experimentally infected with a number of strains of human origin, which were maintained in culture on diphasic media. The rats, which were injected intracaeally with 48-hour cultures, were free of natural infection with *E. muris*. They were killed 7 days later and the contents of the caecum were examined microscopically and by culture, while the condition of the caecum was assessed from macroscopical examination.

Among the strains used, 3 which were isolated from treated relapsing cases produced, in rats, marked ulceration of the caecum. Out of 4 strains which were isolated from untreated carriers, 3 produced no ulceration, though amoebae were numerous in the caeca of the rats, but 1 manifested a degree of virulence comparable to that of strains derived from the acute cases. However, in this case sigmoidoscopy, which had previously been performed on the patient, revealed the presence in the gut wall of healed amoebic lesions: this strain had therefore retained its original invasiveness. The strains of *E. histolytica* studied successfully infected 77 to 100% of rats, but in those belonging to the avirulent group the infection rate was lower than in strains of the virulent group. In the infected rats, the amoebae ingested various micro-organisms and, when lesions were present, elements of the host's tissues and erythrocytes.

Throughout the period of cultivation the peculiarities of these strains remained unchanged, the virulent ones retaining their invasive power and the non-virulent ones not acquiring increased virulence, even after repeatedly completing their full life-cycle *in vitro*. Furthermore, 2 other contact carrier strains remained avirulent after passage from rats to culture and back to rats. The duration of the amoebic infection varied in different rats from 26 to 328 days.

In the therapeutic experiments, various amoebicidal drugs were administered to infected rats in daily oral doses for 6 days. It was found that a 90 to 100%

curative effect could be produced, in rats infected with the virulent strains, with six doses of 4 mg. of emetine hydrochloride per kg. and, in rats infected with avirulent strains, with six doses of 1 to 2 mg. per kg. There was no evidence of specific "emetine resistance". It is true that the strains isolated from acute cases in patients who had been repeatedly treated for relapse were also more resistant to treatment, when transferred to rats, than the strains from carriers, but this resistance was probably correlated with the inherent virulence of such strains. As regards other drugs, it was found that carbarsone, "diodoquin", and chinifoson cured the majority of rats infected with avirulent strains in 6 doses of 125 mg. per kg., and those infected with virulent strains in as many doses of 500 mg. per kg.

On the whole, these experiments have demonstrated "the existence of strains of *E. histolytica* which vary considerably in virulence and in response to treatment". These characteristics appear to be constant, since all attempts to alter the behaviour of the different strains were unsuccessful.

C. A. Hoare

**590. The Pre-erythrocytic Stage of *Plasmodium falciparum***

H. E. SHORTT, N. H. FAIRLEY, G. COVELL, P. G. SHUTE, and P. C. C. GARNHAM. *Transactions of the Royal Society of Tropical Medicine and Hygiene [Trans. roy. Soc. trop. Med. Hyg.]* 44, 405-419, Feb., 1951. 7 figs, 27 refs.

The authors give a complete account of the pre-erythrocytic development of *Plasmodium falciparum*, which was briefly described in a preliminary note 2 years ago.

Of the 2,000 laboratory-bred mosquitoes used in their experiments, 75% were *Anopheles maculipennis* var. *atroparvus* and 25% *A. quadrimaculatus*. After the mosquitoes had fed on a patient infected with a Rumanian strain of *P. falciparum*, when numerous gametocytes were present, dissection of some (30) of the insects revealed an infection rate of 93%. A healthy volunteer (No. 1) was then subjected to the bites of the mosquitoes 3 days in succession, the numbers fed being 350, 95, and 325 respectively (770 bites in all). The infectivity of the mosquitoes was checked by allowing 370 to bite a patient on 4 successive days, after which he developed malaria.

For 3 days following the last exposure to infecting bites the volunteer was subjected to haematological and biochemical tests, and blood films were examined for malaria parasites with negative results. On the next day (140 hours after the first exposure to mosquito bites) laparotomy was performed, and a piece of liver measuring roughly  $\frac{1}{2}$  cubic inch (6.14 c.cm.) was excised and fixed in Carnoy's fluid. One day later (7 days after the first exposure) ring forms of the parasite were found in thick blood films, after which the volunteer underwent a course of treatment which resulted in a radical cure. To determine the time required for the completion of the pre-erythrocytic schizogony and the invasion of the blood stream, a second volunteer was inoculated intravenously with the blood of the first

volunteer 135 hours after the latter had been exposed to mosquito bites. The second volunteer developed malaria 8 days after the inoculation, showing that the pre-erythrocytic development, with the liberation of merozoites, may be completed in less than 135 hours after mosquito transmission of malignant tertian malaria.

Sections of the liver (stained by the colophonium-Giemsa method) revealed stages of schizogony of the parasite which were about 4, 5, and 6 days old, corresponding to infections initiated in the first volunteer by mosquito bites on 3 successive days. All the schizonts were situated within the parenchymatous cells. The 4-day forms are somewhat oval, measure about  $31\ \mu$  in largest diameter, and show a tendency to produce lobose projections. They contain numerous nuclei (some dividing) measuring  $1.5\ \mu$  across. The host cell is only slightly altered, its nucleus being pushed to the periphery. The 5-day schizonts measure  $50\ \mu$  in longest diameter. At this stage the production of lobes is more marked and there is a tendency on the part of the cytoplasm to break up into portions resembling cytomeres. The number of nuclei, which are now smaller (about  $0.8\ \mu$ ), has increased considerably and many are actively dividing. The 6-day schizonts measure upwards of  $60\ \mu$ ; they now form a complicated system of lobes, so that their shape is highly irregular (as shown in an accompanying illustration of a model reconstructed from serial sections through one schizont). At this stage the schizonts have reached maturity: they are segmenting into merozoites measuring about  $0.7\ \mu$  in diameter, and either are ready to rupture or are already releasing merozoites into the surrounding sinusoids. The number of merozoites in a mature schizont is estimated to be 40,000. The parasites are surrounded by a limiting membrane, the nature of which remains unknown. There is no reaction to the presence of schizonts on the part of the liver, but as they increase in size they compress the neighbouring cells. [The appearance of the pre-erythrocytic schizonts is depicted in an excellent coloured plate.]

A comparison with the pre-erythrocytic development of *P. vivax* and *P. cynomolgi* shows that in *P. falciparum* this phase is of shorter duration, merozoites being liberated on the sixth day instead of the eighth day. However, during this period the mature schizont of *P. falciparum* grows to a larger size and produces a much greater number of smaller merozoites. There is also presumptive evidence that—unlike *P. vivax* and *P. cynomolgi*—*P. falciparum* does not continue its development in the tissues beyond the pre-erythrocytic phase.

C. A. Hoare

#### 91. A Study of Gametocytes in a West African Strain of *Plasmodium falciparum*

P. G. SHUTE and M. MARYON. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [Trans. Roy. Soc. trop. Med.] 44, 421-438, Feb., 1851. 11 refs.

This paper deals with the conditions under which gametocytes were produced in a West African strain of *Plasmodium falciparum* which had been passaged in the

course of 17 months through 85 patients at Horton Mental Hospital. Infection was successfully produced by blood inoculation (19), by mosquito bites (24), and by intravenous injection of sporozoites (42). All the patients were given antimalarial drugs and were divided into the following groups according to the treatment received: (A) 24 patients who were treated with sub-therapeutic doses 1 to 12 days after onset of fever and subsequently relapsed; (B) 4 patients who were treated on the fifth day after onset of fever and did not relapse; (C) 12 patients who had a full course of treatment 1 to 5 days after onset of fever and relapsed; (D) 21 patients who had a full course of treatment 1 to 4 days after onset of fever and did not relapse; and (E) 23 patients who were successfully protected by prophylactic drugs. (Since they failed to develop fever or parasites, this group is not considered further.)

In Group (A), gametocytes appeared in the majority (19) of patients: in some, 9 to 14 days after the beginning of the primary attack; in others, 10 to 13 days after recrudescence. Eight of these patients produced infections in mosquitoes (*Anopheles stephensi*); 10 failed to infect any, some because the density of gametocytes was too low, others because only female forms were present. In Group (B), in which the disease was cured, 3 patients showed small numbers of crescents, represented in 2 instances by macrogametocytes only, while in 1 the number was sufficient to produce a slight infection in mosquitoes. In Group (C) treatment was unsuccessful, and all the patients showed numerous crescents 4 to 16 days after recrudescence (26 to 40 days after onset of primary attack). In Group (D) the cure was radical and no crescents developed over a period of 3 months.

The authors note that their findings correspond to the conditions observed in a non-endemic area of falciparum malaria among a non-immune population, in which crescents are produced among persons of various age groups throughout the year. In the present series, 55% of all the cases developed gametocytes in appreciable numbers. Crescents were never found in cases where antimalarial drugs cured the disease in the primary attack, but large numbers invariably developed in cases of recrudescence or relapse after administration of sub-therapeutic doses of antimalarials, which appear to stimulate the production of sexual forms. From these observations it is concluded: (1) that patients leaving hospital should be given a course of a gametocytocidal drug, such as proguanil, between the 14th and 21st days after the last day of fever, and (2) that a clinical and radical cure of a primary attack is of major epidemiological importance in preventing mosquitoes from becoming infected.

In the course of this investigation it was noted that female crescents always appeared before the male crescents and persisted after the latter had disappeared. Evidence is adduced of the development of gametocytes from asexual parasites present in the blood during the remissions between attacks. In view of the importance of determining the sex of gametocytes and the difficulty of differentiating them in thick blood films, a method facilitating their identification in thin films is described.

C. A. Hoare

## IMMUNITY

592. **Cold Agglutinins. VII. Tests for Cold Isohemagglutinins in Pneumonia and other Acute Respiratory Infections over a Four-year Period**

M. FINLAND and M. W. BARNES. *American Journal of the Medical Sciences [Amer. J. med. Sci.]* 221, 152-157, Feb., 1951. 15 refs.

Of 756 patients with pneumonia and other acute respiratory infections tested during a 4-year period, 180 (24%) had cold agglutinins in their serum. Significant titres were 3 times more frequent among the children in the group and in the patients treated at other hospitals than they were in patients treated in the Boston City Hospital. In general, cold agglutinins occurred more often in patients showing clinical or radiological signs of primary atypical pneumonia than in patients suffering from other respiratory diseases. The proportion of patients showing cold agglutinins was highest in the autumn (October to December, 35%), decreased somewhat in summer (July to September, 24%) and winter (January to March, 19%), and was lowest in the spring (April to June, 12%). (The figures are averages over 4 years.) Cold agglutinins occurred in about 33% of patients examined in 1946-7, 16% in 1947-8, 24% in 1948-9, and 26% in 1949-50.

As some of the 756 patients referred to had not been studied in sufficient detail for diagnosis, a group of 123 patients who had been very thoroughly studied were examined: 41 (33%) had cold agglutinins. Of these, 32 showed clinical, radiological, or laboratory features characteristic of primary atypical pneumonia; the remaining 9 also suffered from this disease, but had other respiratory lesions such as pulmonary infarcts or pneumonitis. Eight patients suffering from primary atypical pneumonia had no demonstrable cold agglutinins.

The authors conclude that the cold-agglutinin test is of value in the diagnosis of primary atypical pneumonia, though they admit that the titre may be low, a positive finding transient, and the agglutinins not detectable until late in the disease.

[It would be very interesting to know more about the results in patients from whom several samples were obtained.]

C. L. Oakley

593. **Comparative Studies of the Biological Factors Determining the Antigenic Activity of B.C.G. Vaccine and their Interpretation by Electron Microscopy. (Études comparées des caractères biologiques conditionnant la valeur antigénique du vaccin BCG et leur interprétation au microscope électronique)**

E. GRASSET and V. BONIFAS. *Bulletin der Schweizerischen Akademie der Medizinischen Wissenschaften [Bull. schweiz. Akad. med. Wiss.]* 7, 71-86, Jan., 1951. 12 figs., 5 refs.

Studies were made with the electron microscope on the morphology of B.C.G. vaccine suspensions and of cultures of B.C.G. growing in Dubos's medium. Lyophilized B.C.G. vaccine from the Pasteur Institute, Paris, was found to be composed of cells of normal shape, but with irregular condensations within the cells.

Vaccines for intradermal use from the Pasteur Institute and the State Serum Institute, Copenhagen, were found to contain up to 50% of "ghost" cells; these were attributed to the mechanical damage caused by the grinding of the cultures in the preparation of the vaccine. In Dubos's medium B.C.G. grows with a uniform turbidity, and electron-microscope preparations showed that the greatest cellular uniformity was present after 8 to 10 days' growth.

J. E. M. Whitehead

594. **Constitutional Factors in Resistance to Infection: the Effect of Cortisone on the Pathogenesis of Tuberculosis**

M. B. LURIE, P. ZAPPASODI, A. M. DANNENBERG, and I. B. SWARTZ. *Science [Science]* 113, 234-237, March 2, 1951. 7 refs.

The effect of cortisone on experimental tuberculous infection was studied in 20 littermate rabbits belonging to a strain susceptible to infection with *Mycobacterium tuberculosis* (human type). There were 10 animals in the control and treated groups, the latter receiving 2 mg. cortisone acetate per kg. intramuscularly while the former received suspending medium only. After 3 days' treatment both groups were exposed to infection with the human strain H37 Rv by inhalation. Treatment was continued for 34 to 38 days after infection and then the animals were killed. The treated group showed more numerous pulmonary tubercles of smaller diameter, and also a lesser amount of dissemination from the lungs, than the control group. The pulmonary lesions were found to contain many more bacilli in the treated than in the control group.

J. E. M. Whitehead

595. **Dried Smallpox Vaccine**

J. W. HORNIBROOK and W. H. GEBHARD. *Public Health Reports [Publ. Hlth Rep., Wash.]* 66, 38-43, Jan. 12, 1951. 1 fig., 7 refs.

A method of preparing dried smallpox vaccine is described from the Laboratories of the Michigan Department of Health. One part of vaccine pulp from a calf was mixed with three parts of lactose-salt mixture and ground in a Waring Blender, crystalline benzyl penicillin (penicillin G) being added to make a concentration of 10 units per ml.; 0.5-ml. amounts of this vaccine suspension were freeze-dried in "pyrex" tubes 8 x 110 mm. For individual vaccinations needles were specially prepared by winding linen thread around a roughened area covered by a layer of dried human albumin 0.25 inch (6.35 mm.) from the point; a small drop of vaccine was applied to the linen before freeze-drying. To vaccinate, a drop of 0.5% phenol in water was applied to the skin and the linen cuff on the needle rotated in this to reconstitute the vaccine before scarification.

The hazards of reconstituting dried vaccine, due to powdered pulp being blown out when the tube is broken, are discussed and simple methods of preventing them described. Bacterial counts in the reconstituted vaccine averaged 600 organisms per ml.; the National Institutes of Health maximum standard is 1,000 organisms per ml. Potency tests were carried out on animals and humans with reconstituted vaccine, and on rabbits with the

individually prepared needles; all these tests were satisfactory. [Apparently the oldest vaccine had been stored 113 days at 37° C.] The potency of reconstituted vaccine decreased on standing, and the authors say it should be used on the day of reconstitution.

Peter Story

**596. Diphtheria Antitoxin in Cord-blood. Survey of Samples from 15 Areas of British Isles**

M. BARR, A. T. GLENNY, and H. J. PARISH. *Lancet* [Lancet] 1, 713-716, March 31, 1951. 4 refs.

In order to determine the age at which immunization can be usefully started against diphtheria in infancy, the authors record the results of titrating the antitoxin in 100 samples of blood from the umbilical cord from each of fifteen districts of the British Isles. It was shown by Barr *et al.* (*Lancet*, 1949, 2, 329) that more than 80% of a population of babies born in south-east London were satisfactorily immunized after receiving their first injection of A.P.T. at the age of 3 months. In the present investigation it is shown that highly significant differences exist in the antitoxin content of samples from different localities. Statistically comparable distributions were obtained from 5 industrial towns in the provinces, but these differed considerably from those of the London area. Since there is no constant relation between approximate Shick-positive rates and the number of high-value antitoxin titres obtained in various places, it is assumed that the Shick test cannot provide any reliable guide to the time at which immunization may be usefully started in babies. This period is reckoned as the time when maternally conferred antitoxin has fallen below 0.04 unit per ml. of blood.

Joseph Ellison

**597. Alkali - dissolved Diphtheria Toxoid - Antitoxin Floccules Adsorbed on Aluminium Carriers. Immunization of Adults**

J. H. MASON. *Lancet* [Lancet] 1, 504-507, March 3, 1951. 3 refs.

Investigations on the immunizing properties of dissolved diphtheria toxoid-antitoxin floccules precipitated with potassium alum (P.D.F.) or adsorbed on aluminium phosphate (A.D.F.) are reported. Three groups were tested: probationer nurses aged 17 to 20 years, medical students aged 23 to 30 years, and workers at the South African Institute for Medical Research aged 20 to 40 years. Of the 77 persons given 2 subcutaneous injections of 1 ml. P.D.F. or A.D.F. with an interval of 6 weeks between injections, 2 showed an antitoxin titre of 0.005 unit per ml. of serum, 3 of 0.02 to 0.04, 8 of 0.04 to 0.1, 14 of 0.1 to 0.2, 14 of 0.2 to 0.5, 16 of 0.5 to 1, 17 of 1 to 2, and 3 of >2 a fortnight after the last injection. Of 97 Schick-positive persons, 5 showed a moderate reaction; of 82 Schick-negative persons, 7 showed a moderate reaction. The reactions produced proved much fewer and less severe than those caused by alum-precipitated toxoid or by formal toxoid.

The author advocates the use of A.D.F. or P.D.F. for the immunization of probationer nurses. He advises screening of persons over the age of 6 years before immunization is started, both with Schick and

Schick control tests and with the diluted antigen itself, though A.D.F. and P.D.F. contain little, if any, bacterial protein.

Margaretha Adams

**598. Typhoid and Paratyphoid Endotoxoids in the Prophylaxis of Enteric Fevers. Experience and Collected Results of 15 Years' Immunization (1934-1948). (L'endotoxine typhoparatyphique dans la prophylaxie des infections typhoïdiques. Applications et résultats d'ensemble de quinze ans de vaccination (1934-1948)).**

E. GRASSET. *Revue d'Immunologie et de Thérapie Antimicrobienne* [Rev. Immunol.] 15, 1-4, 1951.

This is a review of 15 years' experience, mainly in South Africa, with typhoid endotoxoid vaccine in the prevention of enteric fever. Prepared according to the technique of the author, it is considered to be a highly potent immunizing agent, while less prone than classical T.A.B. vaccine to cause undesirable after-effects.

After a preliminary controlled trial in which it appeared to be the method of choice, it was successfully used on a large scale to immunize native mine-workers on the Rand—an unstable population living in poor sanitary conditions with enteric fever always present. Following this, its use was extended to other industrial workers, to those engaged in major public works such as irrigation schemes, and to civilians generally. On the outbreak of war in 1939 it was introduced into the Services and later was used for immunizing prisoners of war and civilian internees.

The decreased incidence of enteric fever reported, whether resulting wholly or partly from the use of this vaccine, presents a dramatic picture.

A. D. Macrae

**599. Tetanus Immunization. A Ten Year Study**

J. A. BIGLER. *American Journal of Diseases of Children* [Amer. J. Dis. Child.] 81, 226-232, Feb., 1951. 7 refs.

A ten-year follow-up study of the tetanus antitoxin levels in the blood of 300 children after immunization is reported. After 2 injections of tetanus toxoid, the serum antitoxin levels of 254 of the 262 children reached 0.01 to 35 units per ml. In 8 the levels were between 0.003 and 0.01 unit per ml. All children responded with adequate titres after a booster injection of alum-precipitated toxoid given from 6 months to 10 years after immunization. Children with early 0.01- to 0.1-unit levels followed the same pattern as those with 0.003-unit levels. Protective levels (0.01 to 0.1 unit of antitoxin per ml. of blood serum) could be reached with each of as many as 5 booster injections given up to 10 years after immunization. The response to the booster injection is rapid, occurring within the first 7 days. The greater the number of injections, the longer protective levels are maintained. If 3 injections of tetanus toxoid are given for basic immunization, the third injection really acts like a booster injection. Longer intervals between the injections for basic immunization give higher average titres. The author thinks it advisable to give a booster injection to an immunized person at the time of an injury from which tetanus might develop.

Margaretha Adams

## Paediatrics

### 600. The Blood Sugar Level in Childhood. (Über den Blutzuckerspiegel im Kindesalter)

J. B. MAYER. *Zeitschrift für Kinderheilkunde [Z. Kinderheilk.]* 69, 232-241, 1951. 1 fig., 43 refs.

The blood sugar level in adults varies only slightly. In the newborn a marked decrease takes place, parallel to the loss of weight: values of 6 to 13 mg. per 100 ml. blood have been found without any clinical symptoms. The variations in the blood sugar level in older children are also much greater than in adults.

The blood sugar levels of 25 boys and 25 girls in each of 14 age groups from 2 to 15 years (700 children) were determined by the Hagedorn-Jensen method. Capillary blood was used and the children were fasting. The results are presented in a table and in a graph: the latter shows clearly the increase in the blood sugar level throughout childhood, but there are also two periods of arrest or even decrease. Overweight and underweight children showed identical changes; therefore the variation in the level is not related to hunger, but to the physiological conditions in the respective age groups. Normal growth occurs in four episodes: first to fourth year: first period of mass increase; fifth to seventh year: first period of increase in length; eighth to tenth year: second mass increase; eleventh to fifteenth year: second length increase. During the period of growth in length the total mass of the child changes but little. The blood sugar level is inversely proportional to the intensity of growth, and the infantile "hypoglycaemia" corresponds to the periods of growth in mass.

The total insular apparatus in the foetus, the newborn infant, and the child is three to four times bigger than in the adult, but consists mainly of argyrophil  $\alpha$ -cells. The number of  $\beta$ -cells in each islet is relatively small. The  $\alpha$ -cells produce glucagon, which can be distinguished from insulin and causes breakdown of liver glycogen and increase in the blood sugar level; yet the child is relatively hypoglycaemic because the total number of islets is so large that it balances the scarcity of  $\beta$ -cells per islet, and also because the child with a three to four times higher metabolic rate uses up large amounts of carbohydrate so that the demand balances the supply of carbohydrate. Finally the part played by glucagon is briefly discussed.

Ferdinand Hillman

### 601. The Healthy Child: its Many Disguises

I. GORDON. *British Medical Journal [Brit. med. J.]* 1, 611-614, March 24, 1951. 18 refs.

A plea is made for the recognition that many of the common complaints and findings met with in infant welfare and school clinics interfere with neither health nor development. Treatment in the majority of cases is therefore unnecessary and much public money and doctors' time could thereby be saved. Enlarged tonsils, orthopaedic defects, phimosis, constipation in breast-fed

babies, and innocuous cardiac murmurs form the largest group and are specially discussed. Mention is made of 74 other symptoms and signs which cause anxiety to both parents and unknowing doctors. Included with them are such paediatric problems as the "won't-eat neurosis" and the infant with a stridor. The vexed question "What is health?" is answered as follows: "We are healthy if we (a) feel well, (b) function well, and (c) if the objective signs of imperfection which we all can provide are such as, besides allowing (a) and (b) in the present, give reasonable confidence that we may feel well and function well in the not-too-distant foreseeable future".

David Morris

### 602. Vitamin E Blood Levels in Premature and Full Term Infants

S. W. WRIGHT, L. J. FILER, and K. E. MASON. *Pediatrics [Pediatrics]* 7, 386-393, March, 1951. 2 figs., 12 refs.

Blood samples were taken from infants weighing more than 2.25 kg. on the first or second day of life before the first feed, and also on the fourth and sixth days of life; later, samples were also taken from premature infants weighing between 0.78 and 2.25 kg. and from the mothers of these infants, 28 of whom nursed their babies, while 23 did not. The total tocopherol content of the serum was determined. The tocopherol content of the blood of non-nursing mothers varied between 1.18 and 2.05 mg. per 100 ml., and that of nursing mothers between 1.36 and 1.86 mg. per 100 ml. The values for breast-fed infants were 0.38 mg. per 100 ml. on the 2nd day and 1.46 mg. on the sixth, and the average was 1.35 mg. per 100 ml. of blood at 5 to 8 months. The value for bottle-fed infants was 0.37 mg. per 100 ml. on the second day; it remained relatively steady at about 0.5 mg. per 100 ml. blood up to the fourth month and rose slightly to 0.75 mg. per 100 ml. between the fifth and eighth months of age. The level in premature infants fell steadily from 0.43 mg. during the first 10 days of life to 0.09 mg. per 100 ml. blood at the fortieth day of life.

H. E. Magee

### 603. The Feeding of Premature Infants. The Value of High Caloric Diets in Reducing the Length of Hospital Stay

J. B. HARDY and E. O. GOLDSTEIN. *Journal of Pediatrics [J. Pediat.]* 38, 154-157, Feb., 1951. 2 refs.

The growth of 3 groups of premature infants was compared. Group A, consisting of 47 infants in the Harriet Lane Hospital, were fed on partially skimmed milk with 10% "dextrimaltose", giving a calorie value of 1 Calorie per ml.: of this an amount was given equivalent to 120 to 130 Calories per kg. body weight per day. Group B, consisting of 51 infants, were treated similarly to Group A except that after the first 2 weeks each infant was given as much of the diet as desired. The

calorie intake in this group varied from 121 to 195 Calories per kg. per day. Group C, 47 infants in the Sinai Hospital, were fed half-skimmed milk with 7.5% dextrimaltose, giving a calorie value of 0.85 Calorie per ml. Of this the infant was given as much as was desired from the second or third day. The calorie intake on this regimen varied from 153 to 246 Calories per kg. per day.

The infants in Group C on a "self-demand" regimen made the most rapid weight gains and required the shortest time in hospital. The infants in Group A gained most slowly and remained the longest time in hospital. No ill effects were noted from the self-demand regimen.

Douglas Gairdner

#### 604. The Ectopic Ureter in Childhood, with an Account of Four Personal Cases

A. K. ALLDRED and T. T. HIGGINS. *British Journal of Surgery* [Brit. J. Surg.] 38, 460-466, April, 1951. 14 figs., 16 refs.

#### 605. Possible Role of Pleuropneumonia-like Organisms in Etiology of Disease in Childhood

H. J. CARLSON, S. SPECTOR, and H. G. DOUGLAS. *American Journal of Diseases of Children* [Amer. J. Dis. Child.] 81, 193-206, Feb., 1951. 9 figs., 38 refs.

After a review of the literature on pleuropneumonia-like organisms, the authors present reports of 3 cases in which these organisms may have been of aetiological importance. The first patient was a boy suffering from purpura, soft-tissue swellings, numerous erythematous as well as petechial lesions, and abdominal pain with blood in the stools. He was admitted to hospital because a splinter in his finger had given rise to an indolent ulcer. Three blood cultures, 1 before and 2 after penicillin treatment, proved positive for pleuropneumonia-like organisms. One drop of broth from positive cultures instilled intranasally into 3- to 4-week-old white Swiss mice caused consolidation of the lungs. Cultures made from these lung suspensions revealed the presence of an alpha-haemolytic streptococcus and a pleuropneumonia-like organism. Transfer of the lung suspensions to other mice produced similar lung lesions. No *Streptococcus moniliformis* was found.

The second patient was a boy suffering from intermittent migratory arthritis, abdominal pains, petechial lesions, and soft-tissue and joint swellings. Intussusception made operation necessary. The symptoms had developed 1 week after a human bite. On 13 occasions pleuropneumonia-like organisms were cultured from his blood. Tests were made to determine the sensitivity of this organism to streptomycin, penicillin, sulphadiazine, methylrosaniline chloride, methylene blue, brilliant green, acid fuchsin, and trinitrophenol. No inhibition took place, though the dyes and drugs caused distinct morphological changes.

The third patient was a boy with congenital heart disease who developed a brain abscess with meningitis. Spinal-fluid and blood cultures revealed pleuropneumonia-like organisms before and after treatment with sulphadiazine, penicillin, and streptomycin.

The cultures in these 3 cases were made in brain-heart-infusion broth. The blood cultures were made by the pour-plate technique with tryptose agar containing 1% peptone and 1% dextrose. The staining was carried out in wet mounts with alcoholic methylene blue. The organisms were not classified serologically.

It is noted that the first 2 patients presented chronicity and polyarthritis, characteristics seen so often in animal infections with pleuropneumonia-like organisms.

Margaretha Adams

#### 606. Staphylococcal Infections in Hospital Nurseries and Pediatrics Wards

J. FELSEN, J. LAPIN, W. WOLARSKY, A. J. WEIL, and I. FOX. *American Journal of Diseases of Children* [Amer. J. Dis. Child.] 81, 534-540, April, 1951. 16 refs.

#### 607. Report on Intestinal Parasitism in Children of School Age. (Rapport sur le parasitisme intestinal chez les enfants d'âge scolaire)

F. COUTELEN. *Gazette Médicale de France* [Gaz. méd. France] 57, 857-866, Sept. 15, 1950. Bibliography.

This paper from the Medical School at Lille gives the results of stool and adhesive-cellulose-tape perianal examinations of 6,202 school-children in Northern France. The technique of diagnosis of *Oxyuris* infection by means of "cellophane" tape was that introduced by Graham (Amer. J. trop. Med., 1941, 21, 151). After a discussion of the method of examination employed, the results are presented in two groups as follows: (I) children 2 to 6 years of age at nursery schools; and (II) children in older age groups temporarily resident in institutions.

I. (A) Of 1,586 children 2 to 6 years old at nursery schools (4,384 stools examined), 68.64% were found to be infected. Of these, 27.77% had *Entamoeba coli* and 28.86% *Giardia intestinalis*, and small numbers were infected with seven other protozoa; none had *Entamoeba dysenteriae*. Worms or ova of *Oxyuris* were present in the stools of 21.83% of *Ascaris* in 7.15%, and of *Taenia saginata* in 1.32%. (B) Of 332 nursery-school children from a crowded quarter of Lille examined by 3 stool and 3 cellulose-tape tests, 96.38% had oxyuriasis. (C) Of 3,440 nursery-school children in Lille subjected to one stool examination and one adhesive-tape test, 58.3% were shown to be infected, including 25.7% with *Giardia* and 39% with *Oxyuris*.

II. (A) Of 250 children aged 1 to 15 years in the surgical clinic at Lille, 88% were infected: 20.03% with *Ascaris*, 42.9% with *Trichocephalus*, and 64.5% with *Oxyuris*. Of 49 girls in the last group in whom positive results of the Graham test for oxyuriasis were found, in 77.5% vulval swabs were also positive. (B) Of 160 children aged 2 to 15 years in the medical clinic at Lille, 60.63% were infested with alimentary parasites (including *Oxyuris*). Of 41 girls in this group positive results of the anal test for *Oxyuris*, in 37 positive vulval swabs were also found. (C) Of 100 children aged 1 to 19 years in a residential institution, 98% were infected. The highest percentage of giardiasis occurred among the 2-to-4-year age group; among the older

children 44% had ascariasis, 80% trichocephaliasis, and 75% oxyuriasis. (D) Of 334 children aged 6 to 14 years in a psychiatric institution, 91.31% had oxyuriasis.

The most striking features of the investigation were the general absence of *Entamoeba dysenteriae* and the high incidence of ascariasis among older children in the sanatorium.

There is a valuable list of 177 references to surveys of alimentary infestation carried out in 43 countries.

Ronald MacKeith

**608. Chronic Infection of the Parotid Glands in Children.** (К вопросу о хронических заболеваниях околоушных слюнных желез у детей)

G. V. VOLOBUEVA. *Педиатрия [Pediatrija]* No. 1, 22-24, 1951.

Two cases of chronic parotitis are described in children living in the Moscow area. A girl aged 8 years had, 2 years previously, been in close contact with a case of mumps and had since suffered from recurrent enlargement of the parotid glands accompanied by pyrexia and malaise. At first the attacks occurred at the rate of 1 or 2 a month, but in the last 6 months they had become more frequent and appeared every 4 days, often after eating hard food. On examination, a scanty purulent discharge containing diplococci could be expressed from the parotid duct. No calculi were present. Penicillin was given in a dosage of 200,000 units daily for 4 days and the condition improved, the attacks becoming less frequent. The enlargement of the glands was considered to be due to stenosis of the ducts caused by chronic inflammation. The attacks were at no time typical of mumps, in spite of the history of contact with this condition. In the second case, in a boy aged 10 years, the parotid glands had enlarged periodically since the age of 3, usually when he was in good health, the onset being acute, with pyrexia and swelling of one or both parotids. The glands were firm and painful, and the enlargement persisted for 2 to 6 days. The attacks were often associated with influenza and other minor infections, and were not brought on by eating food of any particular kind. In this case the individual attacks closely resembled mumps.

D. J. Bauer

**609. The Use of Potassium Chloride in the Pre-operative Treatment of Pyloric Stenosis in Infants**

F. M. MATEER, L. GREENMAN, A. C. AUSTIN, J. H. PETERS, H. MERMELSTEIN, F. WEIGAND, and T. S. DANOWSKI. *American Journal of the Medical Sciences [Amer. J. med. Sci.]* 221, 21-27, Jan., 1951. 2 figs., 28 refs.

In this paper from the University of Pittsburgh a study of pre- and post-operative electrolyte balance is reported, made on 6 infants between the second and eleventh weeks of life suffering from vomiting due to pyloric stenosis. By techniques previously described, extra- and intracellular concentrations of sodium and potassium were estimated as well as extracellular fluid, intracellular nitrogen, and blood non-protein nitrogen, chloride, bicarbonate, sodium, and potassium levels.

The following results were obtained. During recovery

from vomiting, retention of sodium, potassium and chloride occurred, but the nitrogen balance remained negative for some time, probably because of lack of milk protein in the early period of treatment. Extracellular sodium content increased markedly, the intracellular sodium content falling: extracellular potassium content rose slightly, and its intracellular concentration also rose. These changes were recorded after the intravenous infusion of sodium and potassium chloride solutions had been started pre-operatively. Blood potassium levels varied.

Comparison with a group of infants kept on potassium-free fluids under similar conditions to those here described revealed that a positive intracellular potassium balance was attained much earlier in those receiving potassium. This return to normal, associated with resumption of normal feeding in the group not receiving parenteral potassium and characteristic of restoration of body fluids and electrolytes to physiological levels, is highly desirable and may be accelerated by potassium administration in these cases. A solution of 35 mEq. of potassium chloride per litre of 5% glucose is recommended.

A. T. Macqueen

**610. Pyloric Stenosis in Twins**

B. W. POWELL and C. O. CARTER. *Archives of Disease in Childhood [Arch. Dis. Childh.]* 26, 45-49, Feb., 1951. 20 refs.

**611. Pyloric Stenosis in Four First Cousins**

C. O. CARTER and T. R. SAVAGE. *Archives of Disease in Childhood [Arch. Dis. Childh.]* 26, 50-51, Feb., 1951. 1 fig., 4 refs.

**612. Adrenal Cortex Extract in Pediatrics. Possible Effect on the Respiratory System of the Newborn**

R. W. PROVENZANO, P. McGOVERN, R. SCHULTZ, and J. HESTER. *American Journal of Diseases of Children [Amer. J. Dis. Child.]* 81, 323-328, March, 1951. 1 fig., 11 refs.

The authors investigated the effect of adrenal cortical extract on the respiratory system of the newborn infant in the Cambridge City Hospital, Cambridge, Mass., and in the St. Elizabeth Hospital, Brighton, Mass. The cases were divided into 3 groups. The first, made up of 40 children, were examined clinically and radiologically. The second, of 336 children, were subjected to clinical examination only. The third group, of 72 infants, was made up of cases of anoxaemia and atelectasis and was uncontrolled. To alternate cases of the first 2 groups 2 ml. of cortical extract containing 50 dog units per ml. was given hypodermically at birth, at 2 hours, and at the sixth hour.

A reduced incidence of rales in the chest was noted in both groups in those children who had received cortical extract as compared with the control series, but in the first group radiology did not show any difference. Of the second group, 24 had well-marked respiratory symptoms, and again those receiving hormone treatment showed a higher incidence, and a more rapid rate, of recovery than the control series. The third group of

babies received adrenal cortical extract, but in some therapy was continued longer than in the other series. The authors noted a satisfactory clinical response, but no comparable untreated series was available for comparison.

[In the control series no information is given as to whether injections of inactive material were given in the same manner as the adrenal cortical extract; if this was not done it is to be wondered whether the stimulation and handling inseparable from such procedures could have affected the results.]

H. G. Farquhar

### 613. Sleep Problems in the First Three Years

R. S. ILLINGWORTH. *British Medical Journal [Brit. med. J.]* 1, 722-728, April 7, 1951. 6 refs.

After commenting on the paucity of literature on this subject, the author gives an outline of his own conclusions and experience. He stresses first the necessity of understanding the normal. After 4 months of age the child acquires sleep habits which may, at 2 or 3 years, develop into a more and more complicated ritual if unchecked. The great variation in the amount of sleep required by different children, and by the same child at different times, is emphasized. The importance of accepting the difficult phase of ego development between 9 months and 3 years is stressed.

After outlining what may be described as the normal routine, which should remain free from regimentation, the possible difficulties are described under 4 headings: bed refusal, sleep refusal, night waking, and early morning waking. The principal factors in the approach to the problem are love and understanding. Firmness must be combined with patience, and a rigid regimen is decried. Drugs are only to be used for a particular purpose, such as breaking a difficult habit due to mismanagement, and only as a last resort. The possible need for treating the mother in order to help the child must be remembered. Each case is an individual problem.

E. H. Johnson

### 614. Spontaneous Subarachnoid Haemorrhage in Children

A. KAHAN. *British Medical Journal [Brit. med. J.]* 1, 567, March 17, 1951. 5 refs.

### 615. Mental Achievement of Congenitally Hypothyroid Children. A Follow-up Study of Twenty Cases

A. TOPPER. *American Journal of Diseases of Children [Amer. J. Dis. Child.]* 81, 233-249, Feb., 1951. 10 figs., 43 refs.

The author studied 20 cretins aged from 2 to 35 years. Thyroid treatment had been begun at from 2 months to 12 years of age, and had been satisfactory as shown by clinical effect, x-ray estimation of bone maturation, and blood cholesterol level in all but 2, including that untreated up to 12 years of age. Good correlation was found between the treatment and physical, skeletal, and sexual development in all the children. Of the 18 cretins adequately treated, 7 had intelligence quotients below 70, 2 from 80 to 89, 7 from 90 to 110, and 2 over 110. Electroencephalograms were recorded satisfactorily from 6

mentally defective cretins and from 6 mentally normal cretins. The latter gave normal records, but 5 of the defectives showed diffuse cerebral dysfunction. The author believes that electroencephalographic investigation in infancy in cretins can be used to foretell the future intelligence level.

G. de M. Rudolf

### 616. A Dietetic Approach to the Coeliac Affection

W. G. WYLLIE, W. W. PAYNE, and D. W. BEYNON. *Archives of Disease in Childhood [Arch. Dis. Childh.]* 26, 4-17, Feb., 1951. 25 figs., 6 refs.

A description is given of the Bircher-Benner fruit and vegetable diet for coeliac disease and of a subsequent modification with added protein. Of 19 patients treated with the unmodified diet, 9 improved, 2 died, and the other 8 improved after dietetic modification. The disadvantages of the original diet were that the period of initial starvation was too long, a fall in plasma protein level occurred and led to oedema, and insufficient vitamin D was provided. The diet was complicated, difficult to prepare, and expensive.

The new diet proposed is divided into four stages. The first, lasting from 1 to 4 days, provides 920 Calories a day, and consists of 5 four-hourly feeds of from 6 to 8 oz. (180 to 240 g.) of "prosol", buttermilk, and glucose, with vitamins A, C, and D added. The second stage, lasting from 4 to 6 days, provides banana purée in addition. The third stage adds starch-free bread, butter, minced chicken, egg custard, and vegetables. The fourth stage introduces starch-containing foods (cornflakes and toast) and provides 1,623 Calories. Vitamin supplements are added separately to all the stages. The protein content of the diet is high, the fat content moderate, and the carbohydrates selected from non-starch-containing foods in the first three stages.

Ten children have been treated with this diet and followed up for 2 to 3 years. The results have been encouraging.

Wilfrid Gaisford

### 617. Some Observations on the Use of Adrenocorticotrophic Hormone in Atopic Dermatitis in Infancy

A. DiGEORGE and W. E. NELSON. *Journal of Pediatrics [J. Pediat.]* 38, 164-168, Feb., 1951. 4 refs.

Observations are reported on 3 infants, aged 7, 5, and 26 months, each of whom had a severe generalized eczema with much itching, resistant to conventional treatment. ACTH was given in doses of 5 to 8 mg. 6-hourly. Within 24 to 48 hours relief from itching was noticeable, and within a few days the skin was obviously greatly improved. Relapses occurred, generally within a few days of discontinuing ACTH, but further remissions could be produced by second or third courses of treatment. An attempt in one instance to prolong the remission by giving small doses of ACTH once or twice daily did not prevent relapse.

It is concluded that ACTH is capable of causing remissions in generalized (atopic) eczema, but that at present this agent has no place in treatment, except possibly as a temporary measure in times of unusual stress.

Douglas Gairdner

## Medicine : General

### 618. Dyshidrosis Produced by General and Regional Ultra-violet Radiation in Man

M. L. THOMSON. *Journal of Physiology* [J. Physiol., Lond.] 112, 22-30, Jan., 1951. 3 figs., 8 refs.

The hypothesis that sunstroke and heatstroke are identical and that the sun acts only by increasing heat load is generally accepted. The author has carried out experiments in the experimental hot rooms at the National Hospital, London, and at the Department of Experimental Psychology, Cambridge, on volunteers. The object of the experiments was to determine whether ultraviolet light radiation (U.V.L.) of the wave-lengths present in sunlight affected men's ability to sweat. Minor's method and quinizarine were used for the qualitative determination of sweating rate on small areas of skin, and Weiner's method, suitably modified, was used for the quantitative estimation of sweating rate.

The results of these experiments show that in a hot, wet environment so arranged as to simulate jungle conditions, general U.V.L. irradiation in moderate erythema doses produced, in 7 persons acclimatized to heat but not to U.V.L., up to 60% diminution in sweating rate on the 2nd or 3rd day after exposure. In 2 subjects, however, similarly irradiated but exposed to a hot, dry environment and high air movement, there was no change in over-all sweating rate.

Since there were no adverse effects on the ability to tolerate heat in any of the above trials, the author concludes that any reduction caused by radiation was at the expense of the wasted sweat only. It appeared that radiation would be beneficial as it would minimize the amount of water and salt loss. By irradiating local areas of skin with a Kromayer lamp the author obtained similar results as with general irradiation. Following a single irradiation the sweating rate fell to a minimum on the 2nd and 3rd day, to rise more slowly to normal. The extent of the reduction and the time taken to return to normal were probably proportional to the amount of irradiation.

M. H. L. Desmarais

### 619. The Cause of Changes in Sweating Rate after Ultra-violet Radiation

M. L. THOMSON. *Journal of Physiology* [J. Physiol., Lond.] 112, 31-42, Jan., 1951. 7 figs., 27 refs.

In a previous paper (see Abstract 618) the author showed that ultraviolet light (U.V.L.) radiation causes a reduction in the total sweat loss of subjects generally irradiated and in the sweating rate of small areas of skin locally irradiated. While searching for the cause of the reduction in sweating the author noted that a vesicular eruption occurred after either local or general irradiation when the subject was tested in a hot room under standard conditions.

On histological examination of the irradiated skin, it was observed that the sweat-gland ducts were blocked,

the lymphatics in the dermis were infiltrated with lymphocytes, and a great many polymorphonuclear cells lay in the capillaries and small vessels. The duct blockage was probably partly responsible for the diminished sweating. This blockage appeared not to be the sole factor responsible for the diminished sweating. Indirect evidence, in fact, suggested that the secretion of sweat itself was reduced and was probably brought about by the toxins which had diffused from the injured epidermis. Skin injury produced by mustard oil also caused a reduction in sweating rate similar in extent to that produced by U.V.L. irradiation. That massive doses of histamine given by iontophoresis failed to produce any significant reduction in sweating was an argument against the reduction induced by U.V.L. and mustard oil being mediated through the release of an H-like substance. The local application of acetylcholine and acetyl- $\beta$ -methylcholine did not cause a return to the normal sweating rate after irradiation.

On comparing the effects of U.V.L. on skins of different colours it was noted that the diminution of sweating in a negro was less marked than in a white man. The difference in melanin pigmentation probably accounted for the relative insensitivity of the negro's sweat function to the effects of U.V.L. radiation.

M. H. L. Desmarais

### 620. Human Immersion and Survival in Cold Water

C. H. WYNDHAM and D. K. C. MACDONALD. *Nature* [Nature, Lond.] 167, 649-650, April 21, 1951. 5 refs.

## ALLERGIC DISORDERS

### 621. Evaluation of Solid ("Dust") Aerosols as Therapeutic Agents

M. S. SEGAL, H. J. RUBITSKY, E. BRESNICK, and L. LEVINSON. *Annals of Allergy* [Ann. Allergy] 9, 53-59 Jan.-Feb., 1951. 3 figs., 16 refs.

The protective action of isoprenaline, aminophylline, and "benadryl" (diphenhydramine) against histamine and methacholine-induced asthmatic attacks has been investigated. The latter substances were given intravenously and their reducing effect on the vital capacity was noted. A protective effect of any of the drugs tested was assumed when the reduction in vital capacity after histamine or methacholine was less than 60% of the reduction occurring in the absence of that drug. Each was tested on at least 4 patients. A 25% isoprenaline dust inhaled in 3 inspirations protected efficiently for 2 hours. This does not differ materially from the effect of the liquid aerosol. Benadryl dust in the same concentration protected against histamine only. Aminophylline dust (260 mg.) had very little effect. Inhalation of penicillin and streptomycin dusts

resulted in blood levels and urinary excretion of a similar order to those obtained with the liquid aerosols, but it is suspected that they may cause sensitivity reactions more easily.

H. Herxheimer

**622. Injections of Massive Doses of Pollen Extract at Three-week Intervals and their Effect on Skin-test Sensitivity**

H. I. SHAHON, A. H. LAPPIN, V. AGRANAT, I. KAMBERG, and F. A. PARISH. *Annals of Allergy [Ann. Allergy]* **9**, 77-84, Jan.-Feb., 1951. 1 fig., 28 refs.

A series of 100 patients with ragweed hay-fever received perennial treatment with 5,000 to 10,000 protein-nitrogen (PN) units every 3 weeks; during the season this interval was shortened to 2 weeks. Clinically, most of these patients experienced relief from this treatment, which was continued for 3 to 4 years. When the skin reaction was retested with 500 PN units after this time, no definite reduction of the wheal was found. This is taken as evidence that the size of the wheal is no indication of the state of hyposensitization.

H. Herxheimer

**623. Experimental, Bronchoscopic, and Anatomical Studies of the Bronchi during Asthma Attacks. (Étude expérimentale, bronchoscopique et anatomique des bronches au cours de la crise d'asthme)**

J. M. DUBOIS DE MONTREYNAUD. *Annales de Médecine [Ann. Méd.]* **51**, 712-764, 1950. 15 figs., bibliography.

Bronchial obstruction was induced in guinea-pigs by inhalation either of histamine aerosols or (after previous sensitization by injection of egg albumen) of aerosols of egg albumen. The external appearance of the attacks of dyspnoea thus caused is the same, but the anatomical changes are different. In the histamine-induced asthma broncho-constriction is dominant and no oedema of the submucous tissue is present; in the egg-albumen-induced asthma such oedema is pronounced; there is eosinophil infiltration, and although the bronchial lumina are narrow, the author is not certain whether this is due to muscular spasm or to the surrounding oedema. [These differences have been described in detail by Kallós and Pagel (*Acta. med. scand.*, 1937, **91**, 292).]

In 12 cases of human asthma, the history of which is given in detail, bronchoscopy and biopsy were carried out. In 5 out of the first group of 6 cases an allergic cause for the asthma was found in the history, and skin reactions were positive in 3. Bronchoscopy was performed during an attack induced by the specific allergen. In all 6 considerable bronchial oedema was found, and hypersecretion was moderate. In the second group of 6 cases no allergic cause was found in the history and the skin reactions were negative. Bronchoscopy was carried out during intercurrent attacks. No oedema was found in these cases, except in one in which it was of an inflammatory nature; hypersecretion was very pronounced and there were signs of bronchospasm. The first group is classed as "allergic asthma", the second as "non-allergic". The conclusion is drawn that allergic asthma is characterized by bronchial oedema,

and non-allergic asthma by bronchial spasm and hypersecretion.

[There is no definite evidence for the absence of allergic factors in the second group if one disregards the negativity of the skin reactions. On the contrary, in 3 there was some eosinophilia. There is therefore no safe foundation for the sharp distinction between allergic asthma caused by oedema and non-allergic asthma without oedema. A more cautious interpretation of this important study is that in some cases of induced allergic asthma mucosal oedema is very pronounced and an obvious cause of the bronchial obstruction, whereas in other cases oedema is absent and hypersecretion more prominent.]

H. Herxheimer

**624. The Problem of Emotional Factors in the Allergies**

S. ROTHMAN and S. A. WALKER. *International Archives of Allergy and Applied Immunology [Int. Arch. Allergy]* **1**, 306-315, 1951. 27 refs.

**625. Effect of Isuprel on Antigen-Antibody and Histamine Skin Reaction**

J. M. SHELDON, J. R. HUSTED, and R. G. LOVELL. *Annals of Allergy [Ann. Allergy]* **9**, 45-49, Jan.-Feb., 1951. 10 refs.

In 13 allergic patients giving positive skin reactions the tests were carried out with dilute substances for intracutaneous injection and with concentrated substances for prick testing. iso-Propylnoradrenaline ("isoprenalin") given sublingually in a dose of 10 mg. decreased the whealing response only if a diluted test substance was used. If it was given as an aerosol in 0.5% solution, the patient taking six inspirations, it had no effect. The histamine-induced wheal was not influenced by isoprenalin given sublingually. [The amounts given by aerosol were so small that no effect could be expected.]

H. Herxheimer

**626. Sudden Death from Asthma**

C. H. A. WALTON, D. W. PENNER, and J. C. WILT. *Canadian Medical Association Journal [Canad. med. Ass. J.]* **64**, 95-102, Feb., 1951. 4 figs., 6 refs.

The authors claim that it is not widely realized that asthma may be a fatal disease. They give short clinical histories with necropsy findings in 13 cases where death was considered to be due to bronchial asthma. Although various clinical types were included, the pathological changes were similar. There was diffuse plugging of the smaller bronchi with mucus in all, and voluminous lungs in 12, accompanied by microscopic emphysema, thickening of the basement membrane of the bronchial epithelium, and eosinophilic infiltration of the bronchial wall in nearly all. Other common changes included splenic eosinophilia and hypertrophy of goblet cells. In 6 cases there was enlargement of the right side of the heart, and one patient died of congestive heart failure.

Important contributory factors appeared to be aspirin sensitivity, the administration of pethidine, morphine, and barbiturates, and the effects of either bronchoscopy or the analgesic preceding it.

K. Gurling

## DIABETES

## 627. The Blood Glutathione Level and its Response to Insulin in Diabetic and Non-diabetic Patients and a Case of Insulin Resistance

R. CAREN and H. O. CARNE. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] 221, 307-313, March, 1951. 17 refs.

The authors discuss the recent interest in the role of sulphur compounds, particularly glutathione, in the pathogenesis of diabetes mellitus. This interest was first stimulated by the discovery that alloxan diabetes in animals could be prevented by glutathione and other sulphhydryl substances such as cysteine.

In the present work 4 groups of cases were studied: (1) 10 normal patients; (2) 42 diabetic patients; (3) 13 patients in the psychiatry wards, some of whom were having insulin therapy; and (4) 1 patient with insulin-resistant diabetes. The normal fasting blood glutathione values were found to be between 26.9 and 41.4 mg. per 100 ml. of blood by the method of Woodward and Fry. The blood glutathione levels were found to be within the normal range except in one diabetic, and there was no significant difference between those who had been receiving insulin and those treated by diet alone. There was a small post-insulin elevation in the blood glutathione levels in Group-(3) patients, which was attributed to haemoconcentration. In the insulin-resistant patient the fasting blood glutathione level was constantly within the normal range.

The authors conclude that the present work does not support the theory that a diminished quantity of glutathione is responsible for impaired function of the beta-cells of the islets of Langerhans in diabetes mellitus. It is pointed out, however, that it does not entirely disprove the theory, as low intracellular glutathione levels may not be reflected in the blood levels.

[The experimental side of this problem has been reviewed by Houssay (*Amer. J. med. Sci.*, 1950, 219, 353), but the importance of the sulphhydryl group in human diabetes is still controversial.]

I. McLean-Baird

## 628. Organic Hyperinsulinism Treated with Alloxan

W. S. L. GILCHRIST and M. J. G. LYNCH. *Lancet* [Lancet] 1, 440-442, Feb. 24, 1951. 5 figs., 14 refs.

A 36-year-old man had suffered from attacks of bilateral lower abdominal pain radiating to the left side of the chest for a period of 31 years, symptoms starting at the age of 5. Thirty-one years after the onset of symptoms he complained of "increasing prostration and night sweats". [The age of onset of these is not mentioned.] The patient continued with typical hypoglycaemic attacks which responded to glucose, but 17.3 g. of alloxan, by mouth and intravenously over a period of 26 days, had no beneficial effects. At necropsy the liver was found to be the site of marked involvement by a "hepatoma of multifocal origin". Secondary neoplastic deposits were present in the ribs. The pancreas showed the changes usual with alloxan therapy and "an abnormal number of islets. Many of these were abnormally large".

The authors regard this case as one of "organic hyperinsulinism due to hypertrophy and hyperplasia of the islets of Langerhans, and later complicated and exacerbated by the development of primary liver-cell carcinoma". [The evidence for this appears to be based on the long history of pain and is open to debate.] The toxic effects of alloxan are listed.

I. Grayce

## 629. Obesity in Diabetes: a Study of Therapy with Anorexigenic Drugs

K. E. OSSERMAN and H. DOLGER. *Annals of Internal Medicine* [Ann. intern. Med.] 34, 72-79, Jan., 1951. 18 refs.

An investigation was carried out at the Mount Sinai Hospital, New York, to test the value of amphetamine compounds in the management of obese diabetic patients. A series of 55 obese diabetics was selected: these patients had previously failed to lose weight on the restricted-calorie diets prescribed for them; 31 patients were on insulin and the remaining 24 were being treated without insulin. They continued to attend as out-patients on a diet of 1,000 Calories daily and were given, in addition, one of the amphetamine drugs: DL-amphetamine sulphate ("benzedrine") was used in the first 3 months of the trial, but thereafter most of the patients had D-amphetamine sulphate ("dexedrine"). The two drugs appeared to have an equal effect in depressing appetite. In 3 hypertensive patients blood pressure increased while they took DL-amphetamine and returned to pre-medication levels when they changed to D-amphetamine.

Of the 55 patients, 36 achieved significant loss of weight (11 to 77 lb. (5 to 35 kg.)). The beneficial effects of losing weight were most evident in the 31 patients who were having insulin before the investigation: 15 were able to discontinue insulin and 11 required a smaller dosage after losing weight. One-third of the patients not having insulin before the trial showed an improvement in glucose tolerance. A follow-up a year after withdrawal of amphetamine revealed that one-third had retained their loss of weight.

K. Black

## 630. A Reconsideration of the Phenomenon of Anticipation in Diabetes Mellitus

A. G. STEINBERG and R. M. WILDER. *Proceedings of the Staff Meetings of the Mayo Clinic* [Proc. Mayo Clin.] 25, 625-630, Nov. 8, 1950. 5 refs.

A series of 100 families in which both a parent and child were affected with diabetes mellitus were studied with reference to age at onset of the disease in successive generations. The so-called "phenomenon of anticipation", which implies that the disease comes on earlier in successive generations and which has been assumed to arise from some kind of "progressive degeneration of the germ plasm", was examined in detail. It was found that the "anticipation" effect could be accounted for adequately by the statistical-biases inherent in the nature of the familial data. There was no reason to believe that it represents any true biological phenomenon.

There appears to be no true correlation between the age at onset of the disease in parents and their children.

Harry Harris

# Cardiovascular Disorders

## ELECTROCARDIOGRAPHY

631. Catheterization of the Left Ventricle in Man. Study of Right Bundle Branch Block by Simultaneous Intracardiac Electrocardiography of Both Ventricles M. F. STEINBERG, A. SELIGMANN, I. G. KROOP, and A. GRISHMAN. *Circulation* [Circulation] 3, 198-201, Feb., 1951. 3 figs., 5 refs.

Simultaneous intracardiac-lead electrocardiograms were obtained from the left and right ventricles in an old man with advanced metastatic carcinoma of the liver and incidental right bundle-branch block. The left ventricular cavity potential was negative throughout. The right ventricular outflow tract cavity potential showed an RSR'S' complex followed by an inverted T wave. The initial R wave synchronized with the first R wave seen in lead V<sub>1</sub> and represented normal activation of the upper part of the interventricular septum from left to right. The onset of the second R wave (R') in the right ventricular cavity lead synchronized with the onset of R' in lead V<sub>1</sub> and represented abnormal activation of the lower part of the septum from left to right, owing to block in the right bundle branch. The final S wave in the right ventricular cavity lead presumably represents final activation of the free wall of the right ventricle, and is represented by the latter half of R' in lead V<sub>1</sub>.

Paul Wood

632. Studies on the Spread of Excitation through the Ventricular Myocardium

R. D. PRATT, H. E. ESSEX, and H. B. BURCHELL. *Circulation* [Circulation] 3, 418-432, March, 1951. 11 figs., 5 refs.

In the isolated perfused dog's heart in which severe lesions limited to the subendocardium were produced, direct-lead electrocardiograms showed that injuries sufficiently severe to produce records of bundle-branch block did not produce any effect which could be ascribed to arborization block secondary to destruction of Purkinje fibres. It was also found that endocardial and epicardial electrodes bore a similar spatial relationship to the spread of excitation through the intervening ventricular wall. In experiments on isolated segments of the ventricular wall of dogs' hearts it was found that the presence of a band of fibres, the long axis of which was parallel to the long axis of the strip, was essential for rapid excitation. It was immaterial whether the fibres were epicardial or endocardial.

On the basis of these two sets of experiments the hypothesis is advanced that the speed at which the excitation process spreads through a given segment of the myocardial syncytium depends on the orientation of the fibres in that segment to each other and to the point of origin of excitation. Endocardial conduction is rapid not because of the presence of Purkinje fibres, but

because the subendocardial bands of myocardium form a network through which excitation can move rapidly along the long axis of the fibres. Spread across the septum in bundle-branch block is slow because excitation is moving through fibres the long axis of which is at right angles to the advancing wave of excitation.

William A. R. Thomson

633. Characteristics of the Unipolar Precordial Electrocardiogram in Normal Infants

R. F. ZIEGLER. *Circulation* [Circulation] 3, 438-443, March, 1951. 4 figs.

Unipolar precordial leads were recorded in 145 normal infants from birth to the age of 3 years. Analysis of these revealed evidence of a normal degree of right ventricular preponderance at this age, as exemplified by large amplitude and late onset of the intrinsic deflection in leads from the right side of the praecordium. The characteristic features of the T wave include upright T waves in V<sub>1</sub> and inverted T waves in V<sub>5</sub> and V<sub>6</sub> during the first 24 hours after birth. During the next 48 to 72 hours there is progressive inversion of T in V<sub>1</sub> and V<sub>2</sub>, and elevation in V<sub>5</sub> and V<sub>6</sub>. In older infants and young children there is slight to moderate elevation of the S-T segment, with multiphasic or inverted T waves in leads from the right and mid-praecordium, and upright T waves in leads from the left praecordium. Emphasis is laid upon the value of these criteria of normality in the diagnosis of congenital heart disease.

William A. R. Thomson

634. The Ventricular Complex in Direct Leads from the Auricles and Great Vessels

F. M. GROEDEL, M. MILLER, and P. R. BORCHARDT. *Experimental Medicine and Surgery* [Exp. Med. Surg.] 9, 48-78, Feb., 1951. 16 refs.

In 4 patients in whom the heart was exposed at operation electrocardiograms were recorded directly from various points on the surface of the heart and great vessels, the indifferent electrode being on the right arm. These records were compared with others made before or afterwards from many points on the chest wall.

The auricular wave from the upper part of the right auricle was deeply inverted, and from the lower part diphasic ( $\pm$ ); these patterns were not, of course, found in chest-wall records. Complexes recorded from the ventricular surfaces had the expected forms (RS over the right, and QR over the left ventricle) except for a narrow transitional zone. Similar patterns, with diminished voltage, were found at points on the chest wall overlying right and left ventricles, but wide areas showed transitional forms, particularly on the front of the chest. Pure "ventricular cavity" patterns—rS from the right and QS from the left ventricles—were not obtained with certainty either from direct or from chest-wall leads.

The conclusion is drawn that unipolar chest and limb lead recordings give the resultant of potential changes occurring over a relatively wide extent of heart surface, and do not merely show what changes occur on that part of heart wall situated perpendicularly beneath the lead.

[The material of this paper is badly presented and difficult to sift.]

J. A. Cosh

**635. The Esophageal Electrocardiogram in the Study of Atrial Activity and Cardiac Arrhythmias**

C. D. ENSELBERG. *American Heart Journal* [Amer. Heart J.] 41, 382-409, March, 1951. 16 figs., bibliography.

Oesophageal electrocardiograms were obtained on 111 occasions in 98 subjects. They were recorded at various levels between 22 and 57 cm. from the anterior nares or teeth, the electrode being introduced through the nose in all cases except 2. The rhythms investigated were: normal sinus rhythm, 36; abnormal sinus rate or rhythm, 6; sinus arrest, 2; A-V rhythms, 4; A-V block (various degrees), 11; premature systoles (various sites of origin), 20; paroxysmal tachycardia, 12; auricular flutter, 9; auricular fibrillation, 12; Wolff-Parkinson-White syndrome, 2. Many of these arrhythmias are illustrated by representative tracings. The distinct and uniform appearance of the P waves in all instances in which there is co-ordinated auricular activity is emphasized. This is of particular importance in the differential diagnosis between auricular tachycardia and auricular flutter, in which other leads are often ambiguous. Seven cases are described in greater detail in order to illustrate the practical value of the method.

A. Schott

**636. The Electrocardiogram in the Tetralogy of Fallot. A Study of 100 Cases. (L'électrocardiogramme dans la tétralgie de Fallot. (Étude de 100 cas))**

E. DONZELLOT, C. METIANU, M. DURAND, A. CHERCHI, and P. VLAD. *Archives des Maladies du Cœur et des Vaisseaux* [Arch. Mal. Cœur] 44, 97-118, Feb., 1951. 14 figs., 17 refs.

The authors analysed 12-lead electrocardiograms from a series of 100 cases of Fallot's tetralogy at the Hôpital Broussais. All patients were operated upon, and 10 came to necropsy; their ages ranged from 2 to 26 years. Abnormally tall P waves were found in 80 cases, generally in both limb and chest leads, though only in certain chest leads in 23. P was never prolonged, and rarely bifid. In 8 of the 10 necropsied cases such tall P waves were recorded, and these 8 were shown to have right auricular hypertrophy. There was right axis deviation in all (+100 degrees or more) and in 93 the angle between the axes of QRS and T was greater than normal (60 degrees). Unipolar limb leads showed that the heart was rarely vertical, and was horizontal in 68; 48 of these had also considerable clockwise rotation. In precordial leads V<sub>1</sub> was mainly positive (R equal to or greater than S) in 90, with the intrinsic deflection occurring at or after 0.03 second. In none was the intrinsic deflection later in V<sub>6</sub> than in V<sub>1</sub>. In all 10 cases right ventricular hypertrophy was found post mortem, the right ventricle forming the anterior and

diaphragmatic surfaces of the heart and often also the apex. The most consistent electrocardiographic indications of this hypertrophy in these 10 cases were, in order of frequency: the intrinsic deflection in V<sub>6</sub> occurring with or before that in V<sub>1</sub>; the electrical axis of the QRS complex beyond +100 degrees; R wave equal to or greater than S wave in V<sub>1</sub>.

J. A. Cosh

**637. The Nature of the RS-T Segment Displacement as Studied with Esophageal Leads. Left Ventricular Hypertrophy**

J. WENER, A. A. SANDBERG, and L. SCHERLIS. *American Heart Journal* [Amer. Heart J.] 41, 410-422, March, 1951. 3 figs., bibliography.

In a previous communication (*Circulation*, 1950, 2, 598), this group of workers showed that in induced coronary insufficiency the RS-T-segment depressions recorded in the precordial leads, and in the oesophageal leads reflecting posterior or diaphragmatic ventricular surface, were regularly associated with RS-T-segment elevations in the oesophageal leads reflecting left ventricular cavity potential—that is, in those recorded at the atrial level. In the present study, in which the same oesophageal electrode with 15 separate terminals mounted 1.75 cm. apart was used, 11 patients with radiological evidence of enlargement of the left ventricle and electrocardiographic changes of left ventricular hypertrophy were investigated by means of standard, unipolar precordial, and oesophageal leads. In all cases the RS-T-segment depressions seen in standard, precordial, and oesophageal leads reflecting potentials of the posterior surface of the heart were associated with RS-T-segment elevations in oesophageal leads reflecting left ventricular cavity potentials. In nearly all cases the depression of these segments was more pronounced in the oesophageal leads reflecting the posterior and diaphragmatic surface of the heart than in the precordial or standard leads. The various explanations put forward in respect of these changes in the RS-T segments are briefly reviewed. It is concluded that in early cases of left ventricular hypertrophy they are probably due to delayed repolarization of the subepicardial layers. In more advanced cases of hypertrophy with superimposed coronary insufficiency, myocardial ischaemia and state of injury are considered to be the most likely aetiological factors. These views are partly based on the changes in the ventricular gradient.

A. Schott

**638. The Normal Esophageal Lead Electrocardiogram**

R. OBLATH and H. KARPMAN. *American Heart Journal* [Amer. Heart J.] 41, 369-381, March, 1951. 4 figs., 24 refs.

The features of the normal oesophageal electrocardiogram were investigated in 40 normal subjects (30 males, 10 females). In 31 persons the heart was in a vertical or semi-vertical position. The electrode employed consisted of 4 small, pear-shaped, brass tips, each measuring 3 to 5 mm., which were passed through a polyethylene catheter of 1.6 mm. (0.067 inch) outside diameter, each soldered to a separate terminal; the tips were permanently fixed 2.5 cm. apart. With this electrode 2 to 4

successive or simultaneous leads could be investigated without moving the electrode. It was paired with Wilson's central terminal as indifferent electrode. The catheter was introduced to a distance of 50 to 55 cm. from the mouth, the tracings being recorded with the subject in the recumbent position. Artefacts were encountered which were due to transmitted aortic pulsation or respiration. The records were arbitrarily classified into high and mid-atrial levels, transitional zone, and ventricular levels. As a rule, those at ventricular levels closely resembled apical precordial leads. In those recorded in the transitional zone (that is, close to the A-V groove) and at atrial levels an intrinsic deflection in the P waves, deep, broad Q waves, smaller R and deeper S waves, and inverted T waves were found. As the exploring electrode approached supra-atrial levels the tracings increasingly resembled those of lead aVR. No differences were found in semi-direct mediastinal records obtained in dogs with brass and nickel-silver oesophageal electrodes. The maximum and minimum duration and amplitude of the several components of the records obtained at various levels are given in tabular form.

A. Schott

**639. Variations in Electrocardiographic Responses during Exercise. Studies of Normal Subjects under Unusual Stresses and of Patients with Cardiopulmonary Diseases**

P. N. G. YU, R. A. BRUCE, F. W. LOVEJOY, and M. E. McDOWELL. *Circulation* [Circulation] 3, 368-376, March, 1951. 4 figs., 11 refs.

Precordial electrocardiograms were taken before, during, and after exercise in 20 normal subjects and in 48 patients with cardiopulmonary diseases. Analysis of the findings was based on changes in the Q-T interval and in the QRS, RS-T, and T waves, and on the presence or absence of premature beats. Whereas on performing standard exercise tests, normal subjects showed no electrocardiographic evidence of coronary insufficiency, in about two-thirds of the patients abnormal changes were demonstrable. Definite RS-T depression and changes in Q-T interval were also observed in normal subjects under unusual stresses. The significant tracing changes were non-specific for any particular group of patients, and since the changes in normal subjects under unusual stress and in patients with disease were indistinguishable from each other it was difficult to differentiate "functional" from "organic" coronary insufficiency.

T. Semple

**HEART**

**640. Acute Nonspecific Pericarditis. Clinical, Laboratory, and Follow-up Considerations**

D. B. CARMICHAEL, H. B. SPRAGUE, S. M. WYMAN, and E. F. BLAND. *Circulation* [Circulation] 3, 321-331, March, 1951. 4 figs., bibliography.

A clinical survey and follow-up of 50 cases of acute non-specific pericarditis is described. The disease occurred at all ages, but 31 of the patients were in the second, third, and fourth decades: 29 patients gave a

history of antecedent upper respiratory infection which preceded the pericarditis by from 1 to 60 days; in over half, however, this interval was 7 to 14 days. In 25 cases the onset was abrupt, and in 46 the initial symptom was pain. This pain was generalized over the front of the chest in 17, localized to the substernal area in 18, to the left shoulder in 6, to the left chest in 3, to the right chest in 2, and to the abdomen in 1. The pain radiated most frequently to the left or right shoulder. The commonest associated symptoms were malaise and fever (49), cough (19), and dyspnoea (18). A pericardial rub was heard within a few hours of onset in the majority of the cases. The heart shadow was enlarged in 25 cases, but in only 3 was this attributable to pericardial effusion. Pleural effusion was found in 14 cases (bilateral in 6, left-sided in 7, and right-sided in 1). Electrocardiographic changes were nearly constant, but might be very evanescent.

Information was available about 41 patients after 2 or more years: 1 had died of hypertension known to have been present for years before the pericarditis: 6 gave a clear-cut history of more than one attack of pericarditis, and 2 had had four recurrences each. In 6 cases electrocardiographic changes had persisted. An x-ray follow-up examination was made on 37 patients; one showed calcification of the pericardium, but the majority were in excellent health.

C. Bruce Perry

**641. Heart Murmurs Recorded Intrathoracically**

F. M. GROEDEL and P. R. BORCHARDT. *Experimental Medicine and Surgery* [Exp. Med. Surg.] 9, 144-147, Feb., 1951. 1 ref.

Phonocardiograms obtained from the region of the apex beat in normal subjects were compared with those obtained later from within pneumothorax cavities in the same subjects (for details of the authors' technique, see *Exp. Med. Surg.*, 1946, 4, 34): three representative pairs of tracings are reproduced and discussed.

Intrathoracic heart sounds had the same duration but lower frequencies than those recorded from the chest wall (50 per second instead of 125 per second). Diastolic murmurs were found intrathoracically that did not show on the chest-wall tracings, and the frequencies of intrathoracic murmurs, systolic or diastolic, were not above 50 per second. The higher frequencies of sounds and murmurs recorded from the chest wall are attributed to their modification by conduction through the tissues within the chest.

J. A. Cosh

**642. The Phonocardiogram before and after Pneumothorax**

P. R. BORCHARDT and F. M. GROEDEL. *Experimental Medicine and Surgery* [Exp. Med. Surg.] 9, 148-160, Feb., 1951. 8 refs.

A series of 4 cases is presented in which phonocardiograms were recorded before and after the therapeutic induction of a left-sided pneumothorax. All initially had systolic murmurs considered to be functional in origin. Tracings after pneumothorax showed a diminution in amplitude of heart sound waves, but no change in their duration or frequency. Systolic murmurs became

briefer or disappeared, and in 2 cases low-frequency diastolic murmurs appeared. In 3, diastolic murmurs were found on the sound recordings made from within the pneumothorax cavity. These alterations are attributed to changes in the surroundings of the heart and great vessels brought about by the pneumothorax, particularly in withdrawal of lung tissue from the aorta and pulmonary artery. No observations were made on the effects of right-sided pneumothorax. *J. A. Cosh*

**643. Beriberi Heart in Iowa Veterans**

**C. H. GUTENKAUF.** *Circulation* [Circulation] 3, 352-362, March, 1951. 5 figs., 15 refs.

A study was made of 5 patients who gave a long history of alcoholism and inadequate nutrition and had congestive heart failure, enlarged hearts with normal rhythm, and signs of peripheral neuritis. Marked clinical improvement and reduction in heart size followed the administration of aneurin. The cardiovascular manifestations of beriberi are discussed, and the importance of its recognition is stressed in view of its reversible nature. *C. Bruce Perry*

**644. Nutritional Heart Disease**

**A. D. GILLANDERS.** *British Heart Journal* [Brit. Heart J.] 13, 177-196, April, 1951. 11 figs., bibliography.

A form of congestive heart failure which is found not infrequently amongst the South African Bantu population is considered to be due to malnutrition. The clinical syndrome differs from the hyperkinetic form of heart disease which has been described as characteristic of beriberi. The clinical and laboratory findings on 30 patients, 22 men and 8 women, aged 30 to 63 years are presented. The usual diet of all patients was markedly deficient, consisting mainly of porridge made from highly refined maize, with white bread, tea, and sugar. The chief characteristics, apart from the usual signs of congestive heart failure, were: (1) extreme degree of generalized oedema; (2) enlargement of the heart, which on x-ray examination was seen to affect the whole heart, giving an enlarged, globular, inert outline; (3) sinus rhythm of the heart, with diastolic gallop; (4) enlargement of the liver. Biochemical investigation of blood showed a moderate degree of hypoproteinaemia, with low albumin values and high globulin values; only in 3 cases were plasma albumin levels less than 3 g. per 100 ml. (the reputed "critical level" for nutritional oedema); haemoglobin and erythrocyte counts were "strikingly normal", but were recorded once only; haematocrit values were "too few to permit of reliable comment"; the fasting blood sugar averaged 77.5 mg. per 100 ml., "which is almost certainly on a lower scale than the normal in the same race".

On treatment with optimum diet alone, without drugs or vitamins, 9 patients made an apparently complete recovery from heart failure within a few weeks and 13 patients made a partial recovery, but relapse readily occurred when the patient reverted to the customary diet; 8 patients died in spite of treatment with diet and drugs (digitalis and mersalyl). No improvement in the condition was observed when the deficient diet

was supplemented with aneurin, vitamin-B complex, brewer's yeast, or  $\alpha$ -tocopherol, nor did any of these treatments enhance the effect of an optimum diet of wholesome food. Liver biopsy in the survivors, and post-mortem examination in the fatal cases, showed an enlarged, diseased liver with haemosiderosis and/or cirrhotic changes, such as is commonly found in the African suffering from prolonged underfeeding.

It would appear that the heart remains free from gross disease for a long time in spite of progressive liver disease; that ultimate heart failure, although a consequence of malnutrition, may be conditioned by primary failure of the liver; and that when the disease has been long established, enlargement of the heart and congestive failure may become irreversible. *Joseph Parness*

**645. Treatment of Enterococcal Endocarditis and Bacteremia. Results of Combined Therapy with Penicillin and Streptomycin**

**W. C. ROBBINS and R. TOMPSETT.** *American Journal of Medicine* [Amer. J. Med.] 10, 278-299, March, 1951. 8 figs., 25 refs.

To 5 patients with enterococcal endocarditis the authors gave penicillin and streptomycin concurrently for periods ranging from 28 to 42 days. The treatment consisted in the intramuscular injection of 500,000 units of crystalline penicillin every 2 hours and 0.5 g. of either streptomycin or dihydrostreptomycin every 6 hours. Permanent arrest of the infection occurred in 4 cases. Although the fifth patient succumbed, it was considered that the infection had been controlled and that death was due to cardiac failure associated with aortic insufficiency. A successful result was obtained in the case of a woman aged 35 years suffering from enterococcal endocarditis and chronic rheumatic valvulitis. No improvement took place after the administration of sulphadiazine and penicillin. Success was achieved, however, with concurrent courses of penicillin and dihydrostreptomycin. The blood became free from bacterial infection 24 hours after the initiation of therapy. Subsequent progress was satisfactory apart from the occurrence of emboli in the femoral arteries. With regard to the management of other cases of enterococcal endocarditis, 2 patients received combined treatment for brief periods before death and a middle-aged woman succumbed despite intensive therapy. A successful outcome was recorded in a young woman who previously had failed to respond to treatment with penicillin and aureomycin. Furthermore, the synergistic action of penicillin and streptomycin was demonstrated by means of experiments *in vitro* on haemolytic enterococci.

Apparently combined treatment is superior to treatment with penicillin alone. It is believed that streptomycin completes the destruction of those bacteria which are only partially inhibited by the action of penicillin. There is no evidence that the drugs combine chemically to produce a more potent compound. As for other antibiotics, further trials are recommended in order to determine the effect of aureomycin and chloramphenicol. Perhaps these substances may prove effective in combination with penicillin and streptomycin. *A. Garland*

**646. Cortisone Therapy in Acute Rheumatic Carditis: Preliminary Observations**

T. N. HARRIS, W. B. ABRAMS, T. F. P. LEO, and J. P. HUBBARD. *Circulation [Circulation]* 3, 215-223, Feb., 1951. 3 figs., 10 refs.

The authors have studied the effects of cortisone therapy in 4 cases of acute rheumatic carditis at the Children's Hospital and General Hospital, Philadelphia. The ages of the patients were 4, 13, 14, and 22 years. The daily dosage of cortisone was 112.5 mg., except for the 4-year-old child, who received 75 mg. daily. The 4-year-old received one course of treatment, the other patients two courses, the duration of a course being about 3 weeks.

Fever subsided in from 1 to 7 days from the beginning of cortisone therapy, except in one case in which the temperature fell slowly during the first course. Joint pains, where present, disappeared within 4 days. In 3 patients congestive cardiac failure developed 4, 10, and 20 days respectively after starting cortisone therapy; this responded well to the usual therapeutic measures while hormone therapy was continued. All cardiac murmurs present at the beginning of treatment were present at the end, and in addition 3 patients developed new murmurs. One patient developed x-ray evidence of cardiac enlargement while under treatment, but 3 patients with initial cardiac enlargement showed no change in this respect.

In one case electrocardiographic abnormalities—elevation of ST segment and inversion of T waves—disappeared during treatment, but inverted T waves returned in the chest leads when cortisone was finally discontinued. In another case there was a prolonged P-R interval which became normal during cortisone treatment, but at the same time the ST segment became progressively elevated as pericarditis developed. The erythrocyte sedimentation rate fell during treatment and failed to return to normal in only one case.

After cessation of the course of cortisone treatment, recrudescence of rheumatic activity occurred in all 4 patients.

C. E. Quin

**647. The Electrokymogram in Wolff-Parkinson-White Syndrome. A Study of Left and Right Ventricular Ejection**

S. DACK, D. H. PALEY, and S. S. BRAHMS. *American Heart Journal [Amer. Heart J.]* 41, 437-447, March, 1951. 4 figs., 32 refs.

The electrokymogram was recorded in 4 patients with the Wolff-Parkinson-White syndrome and correlated with the unipolar precordial, oesophageal, and intracardiac electrocardiogram. The electrokymogram of the aorta and pulmonary artery indicated that ejection from the two ventricles was simultaneous in 2 of the cases and that in the remaining 2 ejection from the right ventricle preceded that from the left by 0.02 second, which is within physiological limits. There was therefore no mechanical ventricular asynchronism in the presence of electrical pre-excitation. Three possible explanations are offered: offset of the premature excitation by slower spread of the impulse through the myocardium of the

pre-excited ventricle; uniform spread of the impulse through the myocardial musculature without any participation of the bundle of His or Purkinje system in either ventricle; or simultaneous premature excitation of both ventricles, with aberrant pathways conducting the impulse from the epicardial surface to the endocardium in both ventricles, again without functioning of the His-Purkinje system.

A. Schott

**648. Hydraulic Formula for Calculation of the Area of the Stenotic Mitral Valve, other Cardiac Valves, and Central Circulatory Shunts. I.**

R. GORLIN and S. G. GORLIN. *American Heart Journal [Amer. Heart J.]* 41, 1-29, Jan., 1951. 5 figs., 34 refs.

A formula for calculating the area of the mitral orifice has been derived from standard hydrokinetic orifice formulae. In its general form the formula is

$$A = \frac{F}{C\sqrt{2gh}}$$

the orifice; F=flow rate in ml. per second; C=empirical constant; g=gravity acceleration; and h=pressure gradient across the orifice. (When this formula is applied to a diseased mitral valve the factor g is the only one which is capable of direct measurement.) This formula has been used to calculate the area of the orifice of mitral valves, tricuspid valves, atrial septal defects, and ventricular septal defect. The constant C has yet to be determined for the aortic valve.

In 6 cases of mitral stenosis the estimated size and the size of the orifice measured at necropsy agreed to within 0.2 sq. cm. The method is put forward as a useful objective test in the evaluation of the effects of valvulotomy.

H. E. Holling

**649. The Phonocardiogram of Aortic Stenosis**

A. LEATHAM. *British Heart Journal [Brit. Heart J.]* 13, 153-158, April, 1951. 10 figs., 3 refs.

**650. Indications for Bishydroxycoumarin (Dicoumarol) in Acute Myocardial Infarction**

H. I. RUSSEK, B. L. ZOHMAN, L. G. WHITE, and A. A. DOERNER. *Journal of the American Medical Association [J. Amer. med. Ass.]* 145, 390-392, Feb. 10, 1951. 9 refs.

Anticoagulant therapy is of value in the treatment of acute myocardial infarction in so far as it reduces the incidence of thrombo-embolism and the number of deaths; in certain types of patient the risk of either might be so small, even without anticoagulant therapy, as to contraindicate its use.

To investigate this possibility, the authors analysed a group of 424 consecutive cases of acute myocardial infarction admitted to the United States Marine Hospital, Staten Island, and the Maimonides Hospital, Brooklyn, none of whom received anticoagulants. Cases were classified as "good risks" or "poor risks", the latter including those who had previous myocardial infarction or who, during their first 24 hours in hospital, had one or more of the following: intractable pain, extreme degree or persistence of shock, significant cardiac enlargement, gallop rhythm, congestive heart failure, auricular fibrillation or flutter, ventricular tachycardia,

intraventricular block, diabetic acidosis, or other serious complicating disease. In the "poor-risk" group (220 cases) there were 17 cases of thrombo-embolism (7.7%) and 98 deaths (44.5%). In the "good-risk" group (204 cases) there were 2 cases of thrombo-embolism (0.98%) and 5 deaths (2.45%); 2 of the deaths occurred within 48 hours of admission and 1 was due to a ruptured ventricle, so that only 2 (0.98%) were regarded as being theoretically preventable.

It is therefore concluded that since anticoagulant therapy with bishydroxycoumarin (dicoumarol) itself carries a perceptible risk, it should be reserved for patients whose prognosis is judged to be unfavourable according to the criteria indicated. *H. McC. Giles*

**651. Effect of Ascending an Ordinary Flight of Stairs on the Work of the Heart. Observations on Normal Individuals and on Patients with Coronary Heart Disease**  
J. A. L. MATHERS, H. I. GRIFFEATH, R. L. LEVY, and J. L. NICKERSON. *Circulation [Circulation]* 3, 224-229, Feb., 1951. 6 figs., 6 refs.

Cardiac output was estimated by means of the low-frequency, critically-damped ballistocardiograph. Cardiac work was calculated in simple units representing the cardiac output in litres per minute multiplied by the mean blood pressure in mm. Hg. The mean blood pressure was taken to be the diastolic blood pressure plus one-third of the pulse pressure.

In 5 normal subjects the cardiac work increased from an average of about 375 units to an average of about 580 units on ascending a flight of stairs at the individual's chosen rate. In 5 patients with ischaemic heart disease the same exercise increased the cardiac work from an average of about 360 units to about 640 units. Descent of the same flight of stairs increased the work of the heart from 420 to 475 units in the control group, and from 360 to 500 in the ischaemic cases. Walking for an equivalent distance on the level produced little change in heart work in the controls, but an increase from 375 to 490 in the ischaemic group. The subject's own speed for performing these tests was usually the optimum in respect of mechanical efficiency; deliberately slowing the speed did not reduce the cardiac work, but rather increased it.

The authors conclude [rather surprisingly] that ascending stairs does not impose a greatly increased burden on the heart, and that the "response of the patient" when ascending stairs is not significantly greater than after descent and only slightly greater than after walking an equivalent distance on the level. *Paul Wood*

**652. The Natural History of Coronary Artery Disease of Long Duration**

E. P. BOAS. *American Heart Journal [Amer. Heart J.]* 41, 323-331, March, 1951. 4 figs., 5 refs.

The author presents an analysis of his case notes of 124 patients with coronary artery disease, all of whom had been under his care for more than 10 years since the onset of their symptoms, but who were otherwise unselected. [Original findings and basis for diagnosis are not given.] There had been no infarction in 26

patients, all the rest having had one or more; in 19 cases the electrocardiogram gave evidence of infarction which had not been recognized clinically. The average length of survival was longer in those patients whose first symptom was angina of effort than in those who began with frank infarction; 81 patients were free of symptoms for one or more years after the onset, and some had no further symptoms after an initial infarct. The incidence of cardiac enlargement, hypertension, and cardiac failure is also dealt with. The author concludes that the course of coronary heart disease is variable and unpredictable.

*A. Venner*

#### CONGENITAL HEART AFFECTIONS

**653. Dynamics of Isolated Pulmonary Stenosis**  
E. N. SILBER, O. PREC, N. GROSSMAN, and L. N. KATZ. *American Journal of Medicine [Amer. J. Med.]* 10, 21-26, Jan., 1951. 4 figs., 8 refs.

A case of pulmonary stenosis investigated in detail by electrocardiography, angiography, and cardiac catheterization leads the authors to conclude that patients with pulmonary stenosis are able to maintain an adequate cardiac output not only at rest, but during ordinary activity. They state that dyspnoea and cyanosis are not common findings in pure, isolated pulmonary stenosis, and appear only during heart failure. The accompanying dilatation and high diastolic pressure in the pulmonary artery is thought to be caused by maldevelopment of the whole pulmonary arterial tree with a decrease in the total number of medium-sized and small branches of the pulmonary artery.

*Henry Cohen*

**654. Cor Triloculare Biventriculatum: an Analysis of the Clinical and Pathologic Features of Nine Cases**

H. M. ROGERS and J. E. EDWARDS. *American Heart Journal [Amer. Heart J.]* 41, 299-310, Feb., 1951. 6 figs., 20 refs.

The authors describe 9 cases of cor triloculare biventriculatum, all from the Mayo Clinic. In 8 the great vessels were transposed, in 2 there was coarctation of the aorta, and in 2 hypoplasia of the aortic arch between the left common carotid and subclavian arteries with patency of the ductus arteriosus. A precordial systolic murmur was noted in most cases, and cyanosis was present in all cases. In one case cyanosis was not observed until the 7th month of life. The age at death ranged from 3 weeks to 8 years.

*D. Verel*

**655. Ebstein's Disease**

C. BAKER, W. D. BRINTON, and G. D. CHANNELL. *Guy's Hospital Reports [Guy's Hosp. Rep.]* 99, 247-275, 1950. 15 figs., 23 refs.

This rare congenital defect of the tricuspid valve, first described by Ebstein, gives rise to a variable clinical picture. Cyanosis, which is usually present, depends on the size of the atrial septal defect, but finger-clubbing and squatting are uncommon, serving to differentiate the condition from Fallot's tetralogy. Palpitation and

reduction of effort tolerance are usual, sometimes with anginal pain. Cardiac enlargement is considerable and is caused principally by a dilated rather than hypertrophied right auricle and ventricle. There is no pulmonary stenosis. Both systolic and diastolic murmurs may be present, but are not constant. Triple rhythm appears to be characteristic of this syndrome and may be explained by the right bundle-branch block and prolonged auriculo-ventricular conduction which often accompany it. Pulsating liver and other signs of tricuspid incompetence may add later to the disability. Death from pulmonary tuberculosis or paradoxical embolism is not uncommon.

The case histories of 2 patients, aged 11 and 17, are here fully reported and analysed in the light of cardiac catheter studies, angiography, and morbid anatomy, and the literature, embryology, and differential clinical diagnosis of the condition discussed in detail.

J. L. Lovibond

**656. Ebstein's Disease—a Case Diagnosed Clinically**

G. REYNOLDS. *Guy's Hospital Reports* [Guy's Hosp. Rep.] 99, 276-283, 1950. 4 figs., 3 refs.

A woman of 33 with limited capacity for exercise and with anginal pain, moderately cyanosed since birth but with no finger-clubbing, showed the following signs: considerable enlargement of the heart, mainly to the left, with triple rhythm, apical systolic and presystolic murmurs, and a split pulmonary second sound. The electrocardiogram showed right bundle-branch block. X-ray studies revealed rather clear lungs, some enlargement of the pulmonary trunk, a large right atrium, and enormous right ventricle with little pulsation and delayed emptying. Although the age of this patient was greater than in similar cases reported previously, these features strongly suggested Ebstein's disease. Hitherto this diagnosis has never been made conclusively during life. The absence of clubbing and squatting argued against Fallot's tetralogy, as also the considerable cardiac enlargement without seriously increasing disability. Atrial septal defect was unlikely when investigations proved a right-to-left shunt and no increase in pulmonary circulation. Pulmonary stenosis was excluded by the diastolic murmur, the split pulmonary second sound, and the absence of a pulmonary systolic murmur.

J. L. Lovibond

**657. Aortic Atresia with Hypoplasia of the Left Heart and Aortic Arch**

S. FRIEDMAN, L. MURPHY, and R. ASH. *Journal of Pediatrics* [J. Pediat.] 38, 354-368, March, 1951. 4 figs., 34 refs.

A description is given of 4 cases of the infantile type of coarctation of the aorta (Evans Type 5; Bramwell Type 3). All patients were male, and all died within a few days of birth, the longest survival being 17 days. Owing to complete or virtually complete obstruction of the aortic orifice, blood from the lungs presumably escaped through the bronchial veins, the left atrium, mitral valve, and left ventricle being diminutive, though normally formed. The right atrium, right ventricle, and pulmonary artery were greatly enlarged and a widely patent ductus supplied

both the descending aorta and the aortic arch, from which the systemic vessels arose in normal fashion. All 4 infants were cyanotic. The electrocardiogram showed tall, sharp P waves and strong right-ventricular preponderance in one case. X-ray examination showed great enlargement of the heart shadow due to the distended right heart; the lung fields looked ischaemic in one case but fairly normal in another. The authors use the term "aortic atresia with hypoplasia of the left heart" to describe the syndrome.

Of 30 similar cases collected from the literature, 18 out of 27 in which the sex was mentioned were male; 24 died within a week of birth, the remainder within 4 months.

Paul Wood

**658. Respiratory Adaptations in Congenital Heart Disease**

J. ERNSTING and R. J. SHEPHERD. *Journal of Physiology* [J. Physiol., Lond.] 112, 332-343, Feb. 20, 1951. 5 figs., 14 refs.

The oxygen dissociation curves of 3 patients suffering from congenital heart disease were found to be within the normal range. All 3 patients showed polycythaemia. The arterial-capillary oxygen-tension gradient was markedly reduced, so that in spite of a reduction of the arterial oxygen tension by as much as 60 mm. Hg, the mean capillary tension was decreased by only 20 to 30 mm. Hg. The main factor responsible for the reduced arterial-capillary tension gradient was the normal shape of the oxygen dissociation curve, whereas the polycythaemia and changes in cardiac output and tissue oxygen utilization appeared to be of less importance.

A. Schweitzer

**659. The Eisenmenger Complex and its Relation to the Uncomplicated Defect of the Ventricular Septum. Review of Thirty-five Autopsied Cases of Eisenmenger's Complex, including Two New Cases**

A. SELZER and G. L. LAQUEUR. *Archives of Internal Medicine* [Arch. intern. Med.] 87, 218-241, Feb., 1951. 9 figs., bibliography.

A report is given of 2 cases of Eisenmenger's complex—one in a man of 57, the other in a woman of 39. Neither appears to have been diagnosed during life, and no physiological or angiographic studies were made. The literature is well reviewed and an analysis of 33 necropsied cases collected therefrom is presented. The size of the defect in the membranous septum was 1 to 3 cm. in diameter, and was thus usually larger than in the *maladie de Roger*. All degrees of overriding have been described, from almost none to complete dextroposition (the aorta arising entirely from the right ventricle). It is pointed out that originally Eisenmenger did not mention overriding of the aorta as part of the syndrome he described, but later he regarded overriding as a functional result of the defect rather than as a developmental dextroposition. It is highly probable that "physiological" overriding of the aorta may occur in an isolated ventricular septal defect when the pressure in the pulmonary artery exceeds that in the aorta. Catheter studies have all revealed extreme

pulmonary hypertension in the Eisenmenger complex, and microscopy has shown changes in the intima and media of the pulmonary arterioles similar to those which are encountered in other forms of pulmonary hypertension.

Cyanosis was always present from birth in cases with complete dextroposition of the aorta, and was usually present in infancy or early childhood in those with partial dextroposition.

The electrocardiogram always showed strong right ventricular preponderance, and the pulmonary artery was always dilated. Systolic murmurs, usually loud and harsh, were commonly present, but varied in location and were less constant than in the *maladie de Roger*.

The prognosis compares well with that of other less serious congenital anomalies. Survival to early or middle adult life is the rule.

Paul Wood

See also Section Radiology, Abstracts 527-8.

## CIRCULATORY DISORDERS

**660. Asymmetrical Arterial Pressures in Cases of Cerebral Hemiplegia, in Hypertension and in Healthy People.** (Асимметрии артериального давления при церебральных гемиплегиях, при гипертонической болезни и у здоровых людей)

A. M. GURVIC. Советская Медицина [Sovetsk. Med.] No. 1, 16-18, 1951.

The author studied the arterial pressures in the shoulder arteries in healthy people and in patients with hemiplegia and hypertension: 8 to 10 readings were taken at rest, simultaneously in both upper limbs, by means of an arterial oscillograph: this was repeated on 3 consecutive days. In 23 healthy people aged 21 to 36 years there was a higher maximum tension on the right side, the difference at times being 25 mm. Hg. The mean difference in maximum tension on the left and right sides was 6.1 mm. Hg: that of the minimum tension was less than 5 mm. Hg. In addition, 7 patients who were left-handed were investigated: 5 had a higher maximum pressure on the left side: the minimum pressures were symmetrical.

There were 20 cases of hypertension, the age of the patients being 30 to 69: 14 had a higher maximum pressure on the right, 4 on the left, and in 2 the pressures were symmetrical. The mean difference between the right and left sides was 1.2 mm. Hg, but in some the difference was as high as 30 mm. Hg. In 9 out of 15 patients with asymmetrical tension a higher minimum tension was present on the left, the mean difference being 6 mm. Hg. There were 49 patients with hemiplegia, aged 20 to 27 years. In 15 the hemiplegia was due to a head injury, in 28 to hypertension, in 4 to cerebral thrombosis, in 1 to post-traumatic arachnoiditis, and in 1 to a cerebral neoplasm: 7 had normal muscle tone, and 15 reduced and 27 raised muscle tone. The duration of the hemiplegia was up to 3 weeks in 15 and

over 3 weeks in 34 cases. In 12 of 15 early cases a higher maximum arterial pressure was present on the paralysed side, and in 28 of the 34 long-standing cases the pressure was higher on the opposite side. The minimum arterial pressure was higher on the paralysed side in 37 cases and did not appear to be influenced by the length of the history.

N. Chatelain

### 661. Intra-arterial and Oral Priscoline. A Clinical Report

J. L. WILSON and E. T. QUASH. *American Journal of Surgery* [Amer. J. Surg.] 81, 336-340, March, 1951. 2 figs., 14 refs.

Peripheral vascular disease of various types was treated in 17 cases with "priscoline" (2-benzylimidazoline hydrochloride), given by mouth and intra-arterially. The average dose was 50 mg. intra-arterially once daily together with 50 mg. orally 4 times daily for a maximum of 21 days. The patient was kept recumbent for an hour after injection. Useful results are claimed in arteriosclerotic ulcers of the leg, in scleroderma, and in chronic thrombophlebitis. All the patients are said to have improved and no less than 14 are said to have been cured.

H. E. Holling

### 662. Comparative Effects of Ether, Alcohol, Tetraethylammonium, and Priscoline in Producing Vaso-dilatation in Peripheral Vascular Conditions

W. J. REEDY. *Journal of Laboratory and Clinical Medicine* [J. Lab. clin. Med.] 37, 365-373, March, 1951. 16 refs.

The vasodilator effect of a number of drugs administered intravenously was assessed by their effect upon the skin temperature of the extremities in patients suffering from peripheral vascular disease. Ether, 0.5 litre of 5% solution, had little or no effect. Ethyl alcohol, 0.5 litre of 5% solution, was followed by a rise in skin temperature in 1 of 2 cases of vasospastic disease, but had no effect in 4 arteriosclerotic cases. Tetraethylammonium, 500 mg., caused slight and inconstant increases in skin temperature. "Priscoline", 75 mg., was followed by a rise in skin temperature to over 31°C. in all vasospastic cases and in 7 of 11 arteriosclerotic cases. In the remainder the vasospastic element was thought to be relieved.

Priscoline is considered to be the most effective of the agents compared. It is suggested that should priscoline fail to cause a rise in skin temperature, mechanical blockage in a blood vessel is probably responsible.

D. Verel

### 663. The Electrocardiogram in Hypertension

A. W. D. LEISHMAN. *Quarterly Journal of Medicine* [Quart. J. Med.] 20, 1-12, Jan., 1951. 14 figs., 12 refs.

An analysis of a series of 218 hypertensive patients is reported; all were below 60 years of age and had diastolic pressures of over 100 mm. Hg, but were otherwise unselected. In 105 the electrocardiogram was normal, while 27 had minor abnormalities and 86 major abnormalities. Major abnormalities, such as T-wave inversions in leads I, II, or V<sub>4</sub>, V<sub>5</sub>, or V<sub>6</sub>, were signi-

fificantly commoner in patients with severe retinal changes, angina, severe diastolic hypertension, and cardiac enlargement. There was no consistent association, however, between any of these findings and the electrocardiographic changes. The changes could not be explained satisfactorily on the sole basis of ventricular fatigue, hypertrophy, or coronary insufficiency.

The progress of a group of 11 hypertensives observed after sympathectomy was considered. It was noted that the electrocardiographic improvement found in 7 could be better associated with gradual reduction in heart size than with the fall in blood pressure.

It is suggested that the electrocardiographic changes of hypertension may be explained best by the occurrence of ventricular hypertrophy out of proportion to the available capillary blood flow, and that they are therefore fundamentally due to myocardial ischaemia. The ischaemia and electrocardiographic abnormalities may be corrected if reduction in ventricular hypertrophy follows sympathectomy.

The electrocardiogram in hypertension should thus be interpreted in relation to the size of the heart. A normal tracing in the presence of an enlarged heart implies a good coronary flow, while an abnormal tracing with a heart of normal size implies an impaired coronary circulation.

J. A. Cosh

**664. The Effect of Vasodilators on the Blood Pressure in Cerebral Hypertension.** (Колебания кровяного давления под влиянием сосудорасширяющих средств при церебральных формах гипертонической болезни)

C. A. LEVINA and M. K. BUKSPAN. Терапевтический Архив (*Terap. Arkh.*) 23, No. 1, 19-21, 1951. 6 refs.

The authors investigated 43 cases of cerebral hypertension by recording the maximum arterial pressure in the temporal, subclavian, and femoral arteries simultaneously by the Riva-Rocci method. Patients were rested for 30 minutes before the investigation, then the blood pressure, pulse rate, and respiration rate were recorded; 2 drops of nitroglycerin (1% in alcohol) were placed under the tongue, and the pulse, respiration rate, and blood pressure were taken at intervals of 5, 15, and 30 minutes. In most cases the blood pressure was only temporarily lowered after nitroglycerin; after 15 minutes it was usually the same as before the administration of nitroglycerin. The maximum arterial pressure in the temporal and subclavian arteries showed a large difference, the subclavian sometimes being twice as high as the temporal. Nitroglycerin appeared to raise the temporal pressure, but did not alter the subclavian pressure appreciably. Comparing the temporal and femoral pressures it appeared that they remained constant before and after nitroglycerin, except in a few cases where the femoral pressure fell and the temporal rose: 2 case histories are given.

The authors suggest that in all cases of cerebral hypertension caution should be exercised in giving vasodilators, as they may lead to a rise in intracerebral blood pressure.

N. Chatelain

## BLOOD VESSELS

### 665. The Cardiac Output in Patients with Arterio-venous Fistulas

J. V. WARREN, J. L. NICKERSON, and D. C. ELKIN. *Journal of Clinical Investigation* [*J. clin. Invest.*] 30, 210-214, Feb., 1951. 1 fig., 24 refs.

The ballistocardiographic method was used in 47 patients with arterio-venous fistula to determine the cardiac output. In as many as 53% there was a significant elevation of the cardiac output of from 25 to 127% above the post-operative (normal) level. In the remaining patients the change in the cardiac output was not significant.

The elevation of the cardiac output could not, in general, be correlated with the size of the fistula or the importance of the leak, nor was there striking correlation with the change in cardiac size, blood volume, pulse rate, and duration of the fistula. It appears that the elevation of the cardiac output does not depend on an increased right atrial pressure, but is related to a change in the peripheral vascular bed. A. I. Suchett-Kaye.

### 666. Effect of Choline upon Experimental Canine Arteriosclerosis

J. D. DAVIDSON, W. MEYER, and F. E. KENDALL. *Circulation* [*Circulation*] 3, 332-338, March, 1951. 4 figs., 16 refs.

Dogs given large amounts of cholesterol in their food and treated with thiouracil develop a severe hypercholesterolaemia, varying degrees of arteriosclerosis, and lipoid infiltration of the liver. Choline was administered in the maximum dose tolerated to dogs receiving large amounts of cholesterol and thiouracil: 3 dogs were treated for 14 months and 6 for 4 months. No difference was observed between the choline-treated and control dogs in the degree of hypercholesterolaemia, arteriosclerosis, or lipoid infiltration of the liver.

C. Bruce Perry

### 667. Peripheral Arterio-venous Aneurysms. A Study of 4 Cases. (Les anévrismes artério-veineux périphériques. Étude clinique et physio-pathologique de 4 cas)

J. LEQUIME, H. DENOLIN, and L. JONNART. *Acta Cardiologica* [*Acta cardiol.*, *Brux.*] 6, 11-23, 1951. 2 figs., 21 refs.

An investigation was made on 4 patients with traumatic arterio-venous aneurysms. In all, cardiac output, as measured by cardiac catheterization, was considerably increased, and this increase explains the cardiac enlargement and the hypertrophy observed. Cardiac output fell to normal in the only case investigated again after a successful operation. Change from the recumbent to the erect position in 2 cases investigated greatly reduced the cardiac output (from 6.03 to 3.63 l. per minute in one case and from 9.04 to 4.30 l. per minute in the other). [Both were cases of aneurysm of the lower extremity, the venous return from which might well be reduced in the erect position.]

Slowing of the pulse following manual compression of the aneurysm (Branham's reaction) was found to be unassociated with any change in right auricular pressure, and therefore not due to a Bainbridge reflex. It is suggested that a carotid-sinus reflex is responsible. [No positive evidence for this view is adduced.]

J. W. Litchfield

**668. Adhesiveness of Blood Platelets in Arteriosclerosis Obliterans, Thrombo-angiitis Obliterans, Acute Thrombophlebitis, Chronic Venous Insufficiency and Arteriosclerotic Heart Disease**

M. E. EISEN, M. C. TYSON, S. MICHAEL, and F. BAUMANN. *Circulation* [Circulation] 3, 271-274, Feb., 1951. 1 fig., 11 refs.

**669. The Effect of Temporary Occlusion of Arterio-venous Fistulas on Heart Rate, Stroke Volume and Cardiac Output**

J. L. NICKERSON, D. C. ELKIN, and J. V. WARREN. *Journal of Clinical Investigation* [J. clin. Invest.] 30, 215-219, Feb., 1951. 1 fig., 14 refs.

This article deals with the changes in heart rate and output occurring during temporary compression of an arterio-venous fistula, as studied by the ballistocardiographic method. In 68% of a group of 25 patients there was a significant decrease in the heart rate (Branham's sign) which occurred almost immediately upon compression of the fistula by the rapid inflation of a sphygmomanometer cuff to 200 mm. Hg. Administration of atropine made this change in pulse rate impossible. In 88% of the patients there was a decrease in stroke volume and cardiac output which was not altered by the use of atropine. To explain Branham's sign a nervous reflex mediated by the vagus must be invoked, the stimulus probably arising from increased arterial pressure. Other observations have suggested that the change in stroke volume was due to variations in diastolic relaxation of the ventricle or to variation in the completeness of systolic emptying.

The operative removal of the arterio-venous fistula produced changes in heart rate and output similar to those following experimental temporary compression of the fistula.

A. I. Suchett-Kaye

**670. The Blood Volume in Patients with Arteriovenous Fistulas**

J. V. WARREN, D. C. ELKIN, and J. L. NICKERSON. *Journal of Clinical Investigation* [J. clin. Invest.] 30, 220-226, Feb., 1951. 3 figs., 21 refs.

The blood volume has been determined in 41 patients before and after operation for the removal of an arterio-venous fistula. The authors have employed an improved technique using the dye T-1824. Changes in blood volume of less than 200 ml. per sq. metre of body surface were not considered significant and were found in 56% of the patients studied. In the remaining 44% the decrease in blood volume after operation ranged from 200 ml. to 1,060 ml. per sq. metre of body surface, thus indicating an abnormally large blood volume in the presence of the fistula. After operative removal of the

fistula the blood volume, if elevated, returned to normal. The increased blood volume in these patients before operation cannot as yet be explained satisfactorily. On the whole, the patients with an elevated blood volume were those with fistulae of the large vessels. The authors have also attempted to correlate the change in blood volume with the duration of the fistula, the cardiac output, and the changes in the size of the heart.

A. I. Suchett-Kaye

**671. Digital Vascular Resistance in Normal, Polycythemic and Hypertensive States**

M. MENDLOWITZ. *Circulation* [Circulation] 3, 694-702, May, 1951. 3 figs., 18 refs.

**672. Treatment of Thrombo-embolic Disease with a Combination of Phenylindanedione and Esculoside. (Le traitement de la maladie thrombo-embolique par l'association phénol-indane-dione et esculoside)**

M. E. LÉVY-SOLAL, J. BADIN, and J. CHOUKROUN. *Gynécologie et Obstétrique* [Gynéc. et Obstét.] 50, 1-10, 1951. 14 refs.

Phenylindanedione is an anti-vitamin K synthesized by Meunier, Mentzer, and Molho in 1947. In animals it lowered the blood prothrombin level by 40% in doses of 10 mg. per kg.; larger doses were not proportionately more effective, and repeated small doses were considerably more effective than a single large one. Kidney damage was not produced with doses of less than 400 mg. per kg. Blood prothrombin levels returned to normal in 48 hours after administration ceased. A diuresis of 3 times the normal output occurred owing to increased capillary permeability. Clinical studies showed the drug to be equally safe and effective in the human subject, and more rapid and reliable than dicoumarol.

In the authors' first 6 cases there were complications, such as cystitis, which were attributed to the drug: these could be avoided, and the effect of phenylindanedione prolonged, by giving esculoside simultaneously. The drugs are given orally: 100 mg. per 20 kg. body weight of phenylindanedione and 10 mg. of esculoside initially, with 200 to 300 mg. phenylindanedione and 20 mg. esculoside the next day. As the effect lasts only for 4 to 5 days, treatment must be repeated every 2 to 4 days in doses depending on the blood prothrombin level. Additional treatment, such as lumbar block for severe pain and antibiotics for infection, was given when necessary. From 50 cases of puerperal thrombophlebitis and pulmonary embolism treated, 6 are selected for description: 2 of severe pulmonary embolism following Caesarian section, 3 of femoral thrombophlebitis, and 1 with a history of 3 previous attacks of phlebitis treated prophylactically. All cases, except one which became bilateral, were cured in 2 to 3 weeks; there were no serious after-effects, and the breast-fed infants were unaffected. It is concluded that anti-vitamin-K therapy for thrombo-embolic conditions may now be used with confidence if the dosage is based on frequent blood prothrombin estimations.

Margaret Puxon

## Disorders of the Blood

### 673. The Treatment of Polycythaemia Vera with Radioactive Phosphorus

B. K. WISEMAN, R. J. ROHN, B. A. BOURONCLE, and W. G. MYERS. *Annals of Internal Medicine* [Ann. intern. Med.] 34, 311-330, Feb., 1951. 7 figs., 16 refs.

This is a report of experience gained in treating 108 cases of polycythaemia vera with radioactive phosphorus during a period of 10 years. The results are contrasted with those in a series of 30 similar cases treated by conventional methods. The aetiology and therapeutic considerations in polycythaemia are considered, and then the method of internal radiation therapy is described. The effect on the symptoms, signs, and haematological picture in this group of cases is described, and the causes of death are discussed. There is a detailed description of the method of using radioactive phosphorus in the treatment of polycythaemia vera. The authors conclude that the method is haematologically sound, effective, inexpensive, and convenient to use. They think that with adequate controls this method of treatment is safe.

John F. Wilkinson

### 674. Cardiac Changes in Cooley's Anaemia and in Subchronic Erythroblastosis. Their Pathogenetic and Diagnostic Significance. (Modificazioni cardiache nella malattia di Cooley e nella eritroblastosi subcronica. Loro importanza patogenetica e diagnostica)

A. LEONE and A. BASCIU. *Annali Italiani di Pediatria* [Ann. Ital. Pediat.] 4, 1-44, Feb., 1951. 23 figs., 23 refs.

The authors review 70 cases of Cooley's anaemia. Cardiomegaly was found in 50 cases, but there was no relation between the duration of the disease, or the erythroblastosis, and the size of the heart. The blood pressure was normal in 80.1%, and in no case was it elevated. Radiography confirmed the clinical findings of cardiomegaly, though there was no particular evidence that right or left preponderance was the more common. The author noted that the increase in heart size in diastole did not seem so great as in normal cases. Oedema was present in many cases, but could be attributed directly to myocardial insufficiency in only 7 cases: in other cases hepatic insufficiency seemed to be a more likely cause. Sixteen of the older children were subjected to a form of test for cardiac function, and in about 80% there was evidence of deficient cardiac response. Digitalis had little effect in any case. Electrocardiography in 11 cases was unhelpful. At necropsy in the 3 fatal cases there were no changes in the pericardium or endocardium, but the myocardium was in all cases abnormal, there being oedema, vacuolization, and fragmentation of fibres, but little evidence of infiltration.

In subchronic erythroblastosis the heart was enlarged in 49 cases out of the 100 studied, though in 14 cases

the enlargement was negligible. There was no relationship between degree of increase and the duration or severity of the disease. The electrocardiogram showed myocardial damage in 8 cases out of 9. Necropsy revealed a similar cardiac condition to that in Cooley's anaemia, though fragmentation was less marked.

The two main findings from this study are the higher incidence of cardiomegaly which occurs in Cooley's anaemia, and the lower incidence of myocardial disease as shown by the electrocardiogram.

J. G. Jamieson

See also Section Radiology, Abstracts 516-17.

### 675. Effect of Cortisone in Sarcoidosis

M. SONES, H. L. ISRAEL, M. B. DRATMAN, and J. H. FRANK. *New England Journal of Medicine* [New Engl. J. Med.] 244, 209-213, Feb. 8, 1951. 6 figs., 8 refs.

Because sarcoidosis in some respects shows similarities to diseases that have responded to the gluco-corticoids, the authors studied the effects of cortisone therapy in this disease. In this paper, which is a preliminary report, a detailed account is given of 2 cases with severe and widespread sarcoidosis in which extended endocrinological studies were carried out. Some evidence of impaired adrenal function was discovered. Cortisone therapy produced marked and steady regression of the lesions, together with amelioration of symptoms.

R. Winston Evans

### 676. Direct Splenic Arterial and Venous Blood Studies in the Hypersplenic Syndromes before and after Epinephrine

C. S. WRIGHT, C. A. DOAN, B. A. BOURONCLE, and R. M. ZOLLINGER. *Blood* [Blood] 6, 195-212, March, 1951. 10 figs., 24 refs.

This is one of a series of studies from the Ohio State University on the various phases of the hypersplenic mechanism. The reservoir function of the spleen may be pathologically increased and therapeutically decreased, with a reversal of the formed elements of the blood sequestered in its pulp-sinusoidal spaces. Figures were obtained from: (1) Blood volume and peripheral blood cell differential studies before and after subcutaneous adrenaline injections. These, in cases of chronic myelogenous leukaemia, demonstrate that the degree of splenic enlargement is a direct function of the abnormal delivery and storage of the granulocytic cells. With treatment, as granulopoiesis in the marrow becomes less dominant, delivery of these cells to the circulation decreases, erythropoiesis increases reciprocally, normal delivery of erythrocytes to the blood is resumed, and the spleen again returns to normal size. In a case of thrombocytopenic purpura, following adrenaline the platelet count rose transitorily from 20,000 to

100,000 per c.mm. with no parallel erythrocyte or leucocyte increase. (2) Splenic arterial and venous blood obtained at laparotomy before and after adrenaline injection into the artery. The subjects were 19 patients with primary hypersplenism (thrombocytopenic purpura, hereditary spherocytosis, and splenic panhaemopenia) and 17 with some constitutional disease involving the spleen. The primarily involved blood-cell elements characteristically entered the spleen in larger numbers than were found leaving this organ. Further, the involved elements tended to be increased in the splenic venous blood after adrenaline-induced contraction. After the surgical removal of all splenic tissue in hypersplenic syndromes, the subcutaneous injection of adrenaline failed to affect significantly the re-established, relatively stable, circulating-cell equilibrium in the blood.

A comparison of the pre-operative adrenaline test with the adrenaline test at laparotomy, made in 2 selected cases, showed that effective cellular mobilization, as interpreted directly from several peripheral blood counts, paralleled closely the direct evidence from splenic venous blood samples.

These findings favour the hypothesis that splenic withholding rather than bone-marrow suppression of blood cells plays the major part in many of the hypersplenic cytopenic states.

Harold Caplan

## ANAEMIA

### 677. Sickling: a Property of All Red Blood Cells

R. ISAACS. *Science [Science]* **112**, 716-718, Dec. 15, 1950. 3 figs., 1 ref.

Those who work with human erythrocytes will know that a variety of forms can be obtained in many varying circumstances. One of these forms, the sickle cell, is not uncommonly seen at the edge of a slide and cover-slip preparation as it slowly dries. The author describes the production of sickle cells by the addition of glue or concentrated gelatin solution to normal blood. Oxygen did not reverse the phenomenon, but dilution generally caused the cells to become spherical and to haemolyse.

E. A. Brown

### 678. Aplastic Anaemia

T. H. BOON and J. N. WALTON. *Quarterly Journal of Medicine [Quart. J. Med.]* **20**, 75-92, Jan., 1951. 3 figs., 31 refs.

The authors review 25 cases of aplastic anaemia seen during the last 10 years at the Royal Victoria Infirmary, Newcastle, and give detailed case histories of 6 which were cured by the repeated transfusion of packed erythrocytes. Neoarsphenamine had been given to one patient, gold injections to 2, but in the other 3 cases no drug was incriminated as the causative agent. Comment is made on: the psychological strain of the repeated transfusions on the patient and the doctor; the frequency of reactions despite careful cross-matching; the value of polythene tubing in reducing phlebothrombosis and venous spasm in restless or nervous patients; and the

routine use of antibiotics to prevent infective complications. In 2 cases intrasternal injections of bone marrow from donors of the same genotype were given with benefit.

Ernest T. Ruston

### 679. The Anemia of Infection. XIII. Studies on Experimentally Produced Acute Hypoferremia in Dogs and the Relationship of the Adrenal Cortex to Hypoferremia

G. E. CARTWRIGHT, L. D. HAMILTON, C. J. GUBLER, N. M. FELLOWS, H. ASHENBRUCKER, and M. M. WINTROBE. *Journal of Clinical Investigation [J. clin. Invest.]* **30**, 161-173, Feb., 1951. 11 figs., 18 refs.

### 680. The Anemia of Thermal Injury. I. Studies of Pigment Excretion

G. W. JAMES, O. J. PURNELL, and E. I. EVANS. *Journal of Clinical Investigation [J. clin. Invest.]* **30**, 181-190 Feb., 1951. 6 figs., 21 refs.

The excretion of pigments in urine and faeces was studied in a series of patients with burns of varying severity. Haemolysis, as judged by increased faecal urobilinogen excretion compared with total circulating haemoglobin, was present in all cases in the first few days after injury. It was greatest in third-degree burns involving more than 20% of the body surface. A remarkable increase was noted in urinary urobilinogen on the third day after injury; this is considered an indication of early hepatic dysfunction. The anaemia associated with burns is thought to be due in part to haemolysis and in part to dyshaematopoiesis dependent on disordered liver function. Oral aureomycin reduces both the faecal and the urinary urobilinogen to small amounts owing to a sterilizing action on the faecal flora. The authors question whether the petroleum-ether-soluble, Ehrlich-reacting substances found after oral aureomycin administration are urobilinogens or whether they are entirely different compounds.

Janet Vaughan

### 681. The Anemia of Thermal Injury. II. Studies of Liver Function

G. W. JAMES, O. J. PURNELL, and E. I. EVANS. *Journal of Clinical Investigation [J. clin. Invest.]* **30**, 191-199, Feb., 1951. 3 figs., 18 refs.

In a study of pigment excretion following severe thermal injury the authors found an increased excretion of urinary urobilinogen, which they interpreted as evidence of liver damage. They therefore undertook an investigation of certain liver-function tests in burned patients, none of whom received sulphonamides or tannic acid or other escharotic therapy. They found that minor to extensive third-degree burns showed an early impairment of liver function as judged by changes in (1) bromsulphalein retention; (2) cephalin-cholesterol flocculation; (3) thymol turbidity; (4) prothrombin time; (5) total protein and albumin-globulin ratio; (6) serum bilirubin level; and (7) urinary urobilinogen content. The most constant changes were found in this last and in the albumin-globulin ratio. Necropsy material in 5 fatal cases showed no constant histopathological

change, but there was evidence of fatty infiltration, cloudy swelling, increased pigments in the reticuloendothelial cells, focal necrosis, and congestion in the liver substance.

The authors suggest that attention should be directed to the prevention as well as treatment of liver dysfunction in severe burns.

Janet Vaughan

682. The Cholinesterase of Erythrocytes in Anemias  
J. C. SABINE. *Blood [Blood]* 6, 151-159, Feb., 1951. 1 fig., 13 refs.

The purpose of the investigation reported was to determine whether or not the increased cholinesterase activity found in the erythrocytes in anaemia is due solely to an increase in concentration of the same enzymes found in normal cells. The investigations were carried out in 4 cases of anaemia from uncomplicated haemorrhage (peptic ulcer), 6 cases of Addisonian pernicious anaemia in relapse, and 4 cases of severe anaemia secondary to cachectic states. It is concluded that the enzyme present in the cells in anaemia is the same as that present in normal cells. Young erythrocytes contain more of the enzyme than old, and its concentration in the erythrocytes is a sensitive index of the activity of erythropoiesis.

A. Brown

683. Observations on the Etiologic Relationship of Achylia Gastrica to Pernicious Anemia. XIII. Hematopoietic Activity of Vitamin B<sub>12a</sub> (Vitamin B<sub>12b</sub>)  
R. F. SCHILLING, J. W. HARRIS, and W. B. CASTLE. *Blood [Blood]* 6, 228-232, March, 1951. 16 refs.

Vitamin B<sub>12a</sub>, formed by catalytic hydrogenation of vitamin B<sub>12</sub>, is also found in liver extracts, often in higher concentration than vitamin B<sub>12</sub> itself.

The hematopoietic activity was tested in 9 cases of Addisonian pernicious anaemia. In 7 cases treated with daily injections of 1, 2, or 4 µg. for 10 to 16 days the maximal reticulocyte response varied from 13 to 27%. In 3 cases vitamin B<sub>12</sub> was given subsequently with no rise, or only an insignificant rise, in the reticulocyte percentage. The authors conclude that vitamin B<sub>12a</sub> is hematopoietically as potent as vitamin B<sub>12</sub>.

In 2 patients given 5 µg. of vitamin B<sub>12a</sub> orally the reticulocyte response was poor, but was potentiated, in 1 patient considerably, when normal gastric juice was added.

John F. Loutit

684. Effect of Citrovorum Factor in Pernicious Anemia  
R. R. ELLISON, S. WOLFE, H. LICHTMAN, V. GINSBERG, and J. WATSON. *Proceedings of the Society for Experimental Biology and Medicine [Proc. Soc. exp. Biol., N.Y.]* 76, 366-370, Feb., 1951. 3 figs., 22 refs.

A series of 6 patients with pernicious anaemia were given daily intramuscular injections of citrovorum factor in doses of 5 to 10 million units (0.75 to 1.5 mg.). Satisfactory clinical and haematological results occurred in 5 cases, the rise in erythrocyte count being optimal in 4. The reticulocyte response, however, was maximal in only 1 patient. The sixth patient showed no response whatever to a dose of 10 million units daily, but subsequently responded to a single injection of 120 µg.

vitamin B<sub>12</sub>. Citrovorum factor when instilled into the sternal marrow did not enhance the maturation of megaloblasts locally, and in this respect it corresponds in action to folic acid in contrast to the local stimulating effect of vitamin B<sub>12</sub>.

Four additional patients with pernicious anaemia were given aminopterin in addition to specific therapy with folic acid and vitamin B<sub>12</sub> in an attempt to inhibit their haematopoietic response; the subsequent administration of citrovorum factor indicated that it is more effective than folic acid in reversing aminopterin inhibition. In 2 patients receiving vitamin B<sub>12</sub> aminopterin exerted no inhibitory effect.

L. J. Davis

685. The Treatment of Acquired Hemolytic Anemia with Adrenocorticotropic Hormone (ACTH)  
W. DAMESHEK, M. C. ROSENTHAL, and L. I. SCHWARTZ. *New England Journal of Medicine [New Engl. J. Med.]* 244, 117-127, Jan. 25, 1951. 5 figs., 30 refs.

A series of 5 patients with severe acquired haemolytic anaemia, all with demonstrable haemagglutinins and a positive Coombs test, were treated with 60 mg. of ACTH daily. Three of the patients had lymphadenopathy. All showed rapid subjective improvement and remission of haemolysis with disappearance of haemagglutinins, though the Coombs test did not change. An improvement in the primary pathological condition in the secondary cases also occurred. Remissions were maintained on reduced doses. The only complications were a tendency to water retention in one and a temporary psychosis in another.

Marjorie Le Vay

686. The Mechanism of Hemolysis in Paroxysmal Cold Hemoglobinuria. I. The Role of Complement and its Components in the Donath-Landsteiner Reaction  
W. S. JORDAN, L. PILLEMER, and J. H. DINGLE. *Journal of Clinical Investigation [J. clin. Invest.]* 30, 11-21, Jan., 1951. 26 refs.

Studies of sera from 2 patients with paroxysmal cold haemoglobinuria (PCH) have shown that large amounts of complement may be necessary for haemolysis in the Donath-Landsteiner reaction. By using an adequate amount of complement, the haemolysins from both patients were found to be stable at 62° C.

An excess of complement is necessary for antibody titration, since a reciprocal relationship exists between the amount of complement present and the antibody titre. Agglutination by antiglobulin serum of erythrocytes sensitized in dilutions of PCH serum provides another measure of antibody level, the titres obtained being comparable to those found by haemolysin titration in the Donath-Landsteiner reaction.

Complement is essential in both the cold and warm phases of this reaction, and there is a reciprocal relationship between the amounts of intact complement required in these two phases. The erythrocyte-PCH antibody system is unique in that it requires complement for antibody fixation as well as for subsequent haemolysis.

The PCH haemolytic system is unusual in another respect, because all components of complement are not necessary for haemolysis. Haemolysis occurs in the

absence of C'1 and C'3. Haemolysis does not occur when C'4 is missing in the cold phase, or when C'2 is missing in the warm phase.

Since only two components of complement are required for haemolysis in PCH, titration of complement in a serum by the sheep cell-ambroceptor system, which requires all four components, may not measure the capacity of that serum to produce haemolysis with PCH antibody.—[Authors' summary.]

**687. The Mechanism of Hemolysis in Paroxysmal Cold Hemoglobinuria. II. Observations on the Behavior and Nature of the Antibody**

W. S. JORDAN, L. PILLEMER, and J. H. DINGLE. *Journal of Clinical Investigation* [J. clin. Invest.] 30, 22-30, Jan., 1951. 15 refs.

Erythrocytes from a patient with paroxysmal cold haemoglobinuria (PCH) were found to be agglutinable in antiglobulin serum (direct Coombs test). Although these erythrocytes had been "sensitized" *in vivo*, they were not haemolyzed when warmed with complement. The cells, however, were haemolyzed, both *in vivo* when the patient was chilled, and *in vitro* when they were chilled and warmed in PCH serum.

The patient's cells were no longer agglutinable in antiglobulin serum 6 hours after *in vivo* haemolysis. No concomitant change in either serum antibody or complement level was detected. Further characterization of the "cell antibody" responsible for agglutination in the direct Coombs test was not possible since the factor could not be demonstrated in eluates from the patient's erythrocytes. The behaviour of the abnormal antibody present in the sera of 2 patients with PCH was studied by using antiglobulin serum (indirect Coombs test) as well as the Donath-Landsteiner reaction. Antibody absorbed *in vitro* from serum with a high antibody titre could be eluted from erythrocytes by heating the cells at 56°C. The PCH serum factor which reacts with antiglobulin serum was identified as the PCH haemolysin.

Fractionation of PCH serum in alcohol-water systems revealed that the PCH antibody is a water-soluble (pseudoglobulin) gamma-globulin and resembles most other human antibodies in this respect.—[Authors' summary.]

**688. Limitation of Hemolysis in Experimental Transfusion Reactions Related to Depletion of Complement and Isoantibody in the Recipient. Observations on Dogs Given Successive Transfusions of Incompatible Red Cells Tagged with Radio-active Iron**

R. M. CHRISTIAN, W. B. STEWART, C. L. YULE, D. M. ERVIN, and L. E. YOUNG. *Blood* [Blood] 6, 142-150, Feb., 1951. 4 figs., 21 refs.

This paper describes experiments designed to assess the importance of depletion of complement and antibody in limiting the rate of destruction of transfused incompatible erythrocytes. The experiments were carried out in dogs the erythrocytes of which lacked the canine A agglutinogen. The cells used for immunization and transfusion contained the A factor and also radioactive

iron, previously administered intravenously to the donor dogs. Each of 4 dogs was given 2 successive transfusions of incompatible dog blood at intervals of 90 or 120 minutes. In each experiment the donated erythrocytes were destroyed much more slowly after the second transfusion than after the first; and the haemoglobinuria produced by the first transfusion was not appreciably increased by the second. The rate of haemolysis was influenced by the initial titre of both antibody and complement.

A. Brown

**689. Six Blood-group Antibodies in the Serum of a Transfused Patient**

R. K. WALLER and R. R. RACE. *British Medical Journal* [Brit. med. J.] 1, 225-226, Feb. 3, 1951. 2 refs.

The authors describe the case of a male negro, aged 30 years, suffering from an undiagnosed collagen disease. During the first week after admission to hospital he was given three blood transfusions of Group-B Rh-positive blood. It was not known whether he had had any previous transfusions. Five days after the third transfusion he became jaundiced and his urine was blood-stained. Six weeks later difficulty was experienced in cross-matching blood for a further transfusion. The patient was then more fully grouped and found to be B, cDe/cde or cDe/cDe, N. His serum was found to contain anti-A, anti-M and anti-S, anti-C, anti-E, and anti-Fy<sup>a</sup>. He was therefore presumably both S- and Fy(a-). The anti-Fy<sup>a</sup> was demonstrated, after absorption, by a positive indirect Coombs test and, unlike previous samples of anti-Fy<sup>a</sup>, also gave a weak positive with Fy(a+) erythrocytes suspended in saline.

G. Jacob

**690. Aetiology of Physiological Jaundice of the Newborn**

A. S. WIENER. *British Medical Journal* [Brit. med. J.] 1, 435-436, March 3, 1951. 14 refs.

It is suggested that physiological jaundice of the newborn is due to the action of auto-agglutinins (cold agglutinins) of maternal origin acting on the cells of the foetus.

G. Discombe

**HAEMORRHAGIC DISEASES**

**691. Effect of Platelet Extract on Hemophilic Blood**  
E. MOND and K. SINGER. *Journal of Clinical Investigation* [J. clin. Invest.] 30, 77-83, Jan., 1951. 24 refs.

Saline-citrate extracts of washed and triturated platelets were prepared and shown to be serum-protein free. Their thromboplastic activity was compared with thromboplastin, the one-stage Quick technique being used. *In vitro*, the extracts were found consistently to reduce to normal the clotting times of the blood of 8 haemophiliacs. The effect on the prothrombin consumption, however, was inconstant and varied from day to day in the same patient. The authors conclude that individual haemophiliacs vary at different times in their ability to produce a sufficiency of thromboplastin.

G. Jacob

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692. The Effect of Orally Administered Desiccated Beef Spleen and Abdominal Lymph Nodes on Megakaryocytopgenesis and Thrombocytes. [In English] E. M. SCHLEICHER. *Acta Haematologica [Acta haemat., Basel]* 5, 143-150, March, 1951. 7 figs., 12 refs.

Dried bovine spleen and abdominal lymph nodes were given in doses of 20 to 80 gr. (1.2 to 3.2 g.) daily by mouth for 10 days to 10 patients with pernicious anaemia in severe relapse, 5 patients with idiopathic thrombocytopenic purpura, 1 patient with chronic myeloid leukaemia with thrombocythaemia, and 4 healthy adult men. Bone-marrow biopsies were made and sections were examined for megakaryocytes. The platelets in the peripheral blood were counted repeatedly. Between the third and fifth days the platelet count rose and the number of megakaryocytes in the marrow increased slightly in patients with pernicious anaemia. In thrombocytopenic purpura and leukaemia the platelet count fell and megakaryocytes in the marrow increased definitely in number.

E. Neumark

693. Splenomegaly in Thrombocytopenic Purpura

L. EHRLICH and S. O. SCHWARTZ. *American Journal of the Medical Sciences [Amer. J. med. Sci.]* 221, 158-168, Feb., 1951. 15 refs.

A series of 110 cases of thrombocytopenic purpura was used to determine the incidence of splenomegaly: in 13 a palpable spleen was found. Two patients developed typical infectious mononucleosis: these recovered spontaneously from their purpura as the splenomegaly subsided. The remaining 11 spleens were removed surgically; 10 showed pathological changes, including Gaucher's disease, infectious mononucleosis, sarcoidosis, lymphosarcoma, congestive splenomegaly, Laënnec's cirrhosis, haemolytic anaemia, and Hodgkin's disease. The only spleen showing splenic hyperplasia without other pathological change came from the youngest patient, a boy of 14. The authors suggest that thrombocytopenic purpura secondary to splenic disease should be called secondary splenogenic thrombocytopenic purpura, that leucopenia is almost constantly present, and that splenectomy is as effective in curing it as it is in primary idiopathic thrombocytopenic purpura. If the spleen is palpable, idiopathic or allergic thrombocytopenic purpura can be excluded.

C. L. Oakley

694. The Alimentary Lesion in Anaphylactoid Purpura

C. L. BALF. *Archives of Disease in Childhood [Arch. Dis. Childh.]* 26, 20-27, Feb., 1951. 2 figs., 23 refs.

The case histories of 5 children suffering from anaphylactoid purpura with alimentary lesions are described: 4 were subjected to operation and the state of the bowel noted. The striking feature was the localized involvement of gut, its intense redness, and the absence of purpura. None of the cases showed any abnormal haemorrhagic tendencies (as evidenced by platelet count, bleeding and clotting time, and Hess's test), although the frequently associated renal lesions suggested capillary damage.

The theory is advanced that there is in these cases a vasospasm with submucosal shunt of blood, diverting

much of the blood in the affected segment, usually the lower ileum, to the outer layers of the gut. The vasospasm and consequent arteriolar anoxia lead to capillary damage, which is not due to a primary anaphylactoid reaction on the capillary endothelium as generally thought.

Wilfrid Gaisford

## LEUKAEMIA

695. The Anti-leukemic Action of Combinations of Certain Known Anti-leukemic Agents

H. E. SKIPPER, J. B. CHAPMAN, and M. BELL. *Cancer Research [Cancer Res.]* 11, 109-112, Feb., 1951. 11 refs.

An apparent anti-leukaemic synergism between urethane and methyl-bis-(2-chlorethyl)-amine had been previously observed, and prompted this study of the possible additive effects of other therapeutic agents known to prolong the lives of mice with transplanted leukaemia. The agents tested included the two mentioned above, benzene, potassium arsenite, colchicine, aminopterin,  $\alpha$ -radiation, 2:6-diaminopurine, and 8-azoguanine. The maximum tolerated dose for 7 successive daily injections of each agent was determined, and from these data combination doses were selected and re-tested for toxicity. Mice of Strain Akm were used, and Strain-Ak4 leukaemia, which kills untreated mice in 7 to 12 days.

Large groups of mice received intraperitoneal inoculations of 0.1 ml. of leukaemic spleen pulp, and 2 days later groups of 10 were injected with the appropriate dose of one of the above agents or a combination of them. The results of over 60 experiments are tabulated, and the effectiveness of the treatments expressed as the percentage increase in survival over untreated controls. Only urethane with nitrogen mustard showed synergistic activity, and even in this case the anti-leukaemic effect was less than that of aminopterin or a-methopterin.

H. G. Crabtree

696. Titrated, Regularly Spaced Radio-active Phosphorus or Spray Roentgen Therapy of Leukemias

E. E. OSGOOD. *Archives of Internal Medicine [Arch. intern. Med.]* 87, 329-348, March, 1951. 6 figs., 26 refs.

The author outlines the methods used for 9 years in the treatment of chronic leukaemia. Before 1947 "spray" irradiation of the whole body was used, and since 1947 radioactive phosphorus. The dose was determined by the initial response of the patient, and thereafter an attempt was made to keep the dose constant and to control therapy by varying the interval between treatments. The objects of treatment are to enable the patient to lead an active life, to maintain the leucocyte count at about 10,000 to 20,000 cells per c.mm., to maintain body weight, to prevent anaemia, and to control enlargement of liver, spleen, and lymph nodes. Small, frequent treatments are preferable, but when using radioactive phosphorus, intervals of less than 4 weeks should be avoided because of the danger of cumulative effects. Local irradiation of lymphoid masses was attempted only twice, and the spleen was only once removed for secondary haemolytic anaemia.

On this regimen the mean duration of life after the onset of the disease was 4 years for myeloid leukaemia (20 cases) and 3.4 years for lymphatic leukaemia (38 cases), but there was great individual variation.

[It is difficult to outline a definite therapeutic drill of this kind. As the disease progresses some of the stated objects of treatment will become unattainable and others may conflict. In chronic lymphatic leukaemia, at least, the clinical state of the patient is probably a more important guide to therapy than the leucocyte count.]

P. C. Reynell

**697. Familial Leukemia. A Report of Leukemia in Five Siblings, with a Brief Review of the Genetic Aspects of this Disease**

R. C. ANDERSON. *American Journal of Diseases of Children* [Amer. J. Dis. Child.] **81**, 313-322, March, 1951. 1 fig., 11 refs.

The author describes a family in which 5 children of one generation were affected by leukaemia. Brief clinical summaries are included, as well as a reference to similar cases in the literature. One child was observed for 2 years before the typical findings were demonstrated in the blood, another for over 1 year; 3 unaffected siblings were observed; 1 showed a leukaemoid picture in the blood, associated with a respiratory infection, which was confirmed by examination of the bone marrow. Necropsy following another respiratory infection did not show evidence of leukaemia. The blood examinations of the parents and the other 2 siblings were normal. Questioning of 135 members of the family revealed only one case of cancer, and none of blood disorder.

H. G. Farquhar

**698. The Haemolytic Factor in the Anaemia of Lymphatic Leukaemia**

G. M. BROWN, S. M. ELLIOTT, and W. A. YOUNG. *Journal of Clinical Investigation* [J. clin. Invest.] **30**, 130-136, Feb., 1951. 3 figs., 21 refs.

The results are described of an investigation of the survival of transfused erythrocytes in patients with lymphatic leukaemia by Dacie and Mollison's modification of Ashby's technique. The results are expressed numerically in the manner previously described by Brown and his associates, which enables an analysis of the type of haemolytic mechanism involved to be made. In 3 of the 4 cases studied the transfused cells were destroyed at a rate faster than normal; this was interpreted as evidence of excessive haemolysis. Urethane was being taken in one of these. In 2 cases there was evidence of the exponential haemolytic process which is not found in normal recipients.

The authors conclude that in at least some cases of lymphatic leukaemia the anaemia is contributed to by increased haemolysis, even though other evidence of this, a raised serum bilirubin level or a raised reticulocyte count, is lacking. The survival rate of transfused cells, they suggest, is perhaps a more delicate method of detecting increased haemolysis than those usually adopted. In addition to increased haemolysis they also suggest that in at least certain cases of lymphatic leukaemia there is abnormal haemolysis. The anaemia of lymphatic leukaemia, the authors conclude, is partly haemolytic and partly dyshaematopoietic.

Janet Vaughan

**699. Experimental Meningo-encephalitis in the Rabbit after Intracerebral Injection of Filtered Leukaemic Material. Presence of Intracellular Bodies in the Brain.** (Méningo-encéphalite expérimentale du lapin après injection intracérébrale de produits leucémiques après filtration. Présence de corpuscules intracellulaires dans le cerveau)

M. PETZETAKIS. *Presse Médicale* [Pr. méd.] **59**, 388-389, March 28, 1951. 4 figs., 11 refs.

After filtration, defibrinated blood from 2 cases of acute leukaemia and 3 cases of myeloid leukaemia was inoculated intracerebrally into rabbits. A type of encephalitis which the author regards as pathognomonic developed, a striking feature being the presence of intracellular structures of the same type as those sometimes seen in immature cells in the course of acute leukaemias. Inoculation of the same substance heated to 56° C. for 20 minutes always gave negative results. It is concluded from this that leukaemia is almost certainly due to a filter-passing virus.

A. Piney

**700. Erythroleukaemia**

E. K. BLACKBURN and L. G. LAJTHA. *Blood* [Blood] **6**, 261-269, March, 1951. 2 figs., 12 refs.

The results are reported of marrow culture in a case of progressive, unresponsive anaemia in a man of 27 with peripheral leuco-erythroblastosis. The sternal marrow was cellular, with a considerably lowered leuco-erythrogenetic ratio (0.42) and a relative myeloid predominance of early forms and of atypical blast cells. No megaloblasts were seen. Culture showed delayed maturation rates for erythroid and myeloid tissues, especially the former. The abnormally large number of basophilic normoblasts decreased without any corresponding rise in the number of more mature forms. The proportions of freely extruded nuclei and smear cells in the cultures were high; the extruded nuclei showed an unusually high resistance and stability, indicating that nuclear maturation was disturbed qualitatively: The patient's serum produced normal maturation in a normal marrow.

The authors point out that when an abnormal normoblastic maturation rate is found, a qualitative, probably neoplastic, change in the nature of these cells is suggested, since the same changes may be found in the myeloid series in cases of myeloid leukaemia. Hence marrow culture may prove of diagnostic value in differentiating between a true aplastic anaemia, an aplastic initial phase of leukaemia, and the mixed forms of the erythroleukaemic group.

Harold Caplan

**701. Aleukaemic Myeloid Leukaemia Presenting as Aplastic Anaemia**

A. B. BLACK and M. J. MEYNELL. *British Medical Journal* [Brit. med. J.] **1**, 1430-1431, June 23, 1951. 2 refs.

## Respiratory Disorders

### 702. Diffuse Bilateral Fibrocystic Disease of Lungs (Honey-comb Lungs)

L. HYDE, B. HYDE, and C. POKORY. *Diseases of the Chest [Dis. Chest]* **19**, 190-200, Feb., 1951. 5 figs., 4 refs.

The authors report 4 cases of diffuse bilateral fibrocystic disease of the lungs; 2 of the patients are still alive and are at present asymptomatic; these cases are therefore unproven. The disease is differentiated from cystic emphysema in that it occurs in younger patients, usually males, is bilateral, and often leads to secondary effects in the lungs (spontaneous pneumothorax) and heart (cor pulmonale), and to sudden death. The lesion may be congenital or acquired. Treatment is unsatisfactory and the ultimate prognosis is poor.

A. Ackroyd

### 703. Pulmonary Involvement in "Febrile Catarrh". (Lungemanifestationer ved "febris catarrhalis")

T. CHRISTIANSEN and V. SCHMIDT. *Nordisk Medicin [Nord. Med.]* **45**, 593-598, April 18, 1951. 20 refs.

A series of 647 cases admitted to the Military Hospital, Copenhagen, with the diagnosis of "catarrhal fever" (or influenza) are reviewed: 70 of these were subsequently diagnosed as specific conditions such as tonsillitis, scarlet fever, or bronchitis. Of the remaining 577, 40% showed some involvement of the lungs, which in over half was silent and would probably not have been diagnosed but for routine x-ray examination. There were 8 cases of pulmonary tuberculosis, 2 of which were sputum-positive, without radiological evidence. Only 43 cases could be identified as due to influenza A or B, and comprehensive bacteriological and serological investigations were inconclusive in the remainder. The authors believe that they were caused by a hitherto unidentified virus.

W. G. Harding

### 704. Incidence of Lipoid Pneumonia in a Survey of 389 Chronically Ill Patients

W. VOLK, L. NATHANSON, S. LOSNER, W. R. SLADE, and M. JACOBI. *American Journal of Medicine [Amer. J. Med.]* **10**, 316-324, March, 1951. 7 figs., 29 refs.

Patients suffering from chronic diseases such as Parkinsonism and rheumatoid arthritis were investigated for the presence of lipoid pneumonia. In 50 of 389 cases there was a history of mineral-oil therapy, either by the oral route or by nasal instillation. The duration of therapy ranged from a few weeks to several years: 4 patients had bronchiectasis and 27 patients complained of cough. On examining the chest the investigators detected moist rales in 20 cases. With regard to special procedures, fat was eliminated from the dietary and the sputum was examined for lipophages and for free lipoid material. Sputum tests indicated that 55 patients

were suffering from lipoid pneumonia. Two more cases were diagnosed when other methods of investigation were employed. In all but 3 instances the diagnosis was confirmed by examining material aspirated from the lungs. On radiological examination of the chest a diagnosis of lipoid pneumonia was made in 20 patients with a "ground-glass" appearance of the lower lobes and in 13 patients with retrocardial and peribronchial infiltration. Post-mortem examination revealed the presence of the disease in 5 cases.

The authors point out that mineral oil may be aspirated into the lungs even when the cough and swallowing reflexes are intact. Oil medication must be discontinued as soon as the diagnosis of lipoid pneumonia is established. Nevertheless, aspiration of disintegrated lipophages may produce progressive changes despite the cessation of oil therapy. The condition must be differentiated from bronchogenic carcinoma, bronchiectasis, and pulmonary infections. When the lesions are circumscribed, skiagrams of the chest may reveal shadows which simulate those of pulmonary neoplasms. Bronchography may be of value in such circumstances. It is noteworthy that although postero-anterior views may fail to show any radiological evidence of oil aspiration, the lesions may be revealed by lateral and oblique views or by over-exposing the x-ray films.

A. Garland

### 705. Primary Atypical Pneumonia with High Titer of Cold Hemagglutinins, Hemolytic Anemia, and False Positive Donath-Landsteiner Test

F. L. NEELY, W. H. BARIA, C. SMITH, and C. F. STONE. *Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.]* **37**, 382-387, March, 1951. 3 figs., 13 refs.

The authors discuss in detail the case of a 30-year-old white woman admitted to Piedmont Hospital, Atlanta, Georgia, in 1947 suffering from severe primary atypical pneumonia involving both lungs. She was placed in an oxygen tent at 68° F. (20° C.), allowed large amounts of iced beverages to drink, and given penicillin. Six days after admission the pneumonia showed signs of resolution, but the skin was slightly icteric. On the tenth day the patient was extremely weak and complained of aches in the back and legs. There was enlargement of the liver, with tenderness over the spleen. The icteric index was 80 units, haemoglobin 5 g. per 100 ml. of blood, erythrocyte count 1,430,000 per c.mm., and leucocyte count 45,750 per c.mm., with immature leucocytes of myeloid type. The cold haemagglutinins were positive in 1 in 4,096 dilution, and the erythrocytes in the test haemolysed after being brought to room temperature. Five transfusions of blood were given, difficulty being experienced in cross-matching the blood. Agglutination occurred at room temperature, but not at incubator temperature. The Donath-Landsteiner test was reported as positive; it was later repeated with guinea-pig

serum as complement and (as described by Kolmer) without complement, and was "slightly positive", haemolysis being incomplete and thus indicating the presence of haemagglutinins rather than true haemolysins. By the thirteenth hospital day the jaundice had subsided and leucocyte count was normal; a week later the cold agglutinins were positive in 1 in 128 dilution. The patient's subsequent recovery was uneventful.

The authors conclude that in the treatment of patients with primary atypical pneumonia with a high titre of cold haemagglutinins certain precautions should be taken: avoidance of chilling (by cold oxygen tent, sponging, cold air, cold drinks, or antipyretics); use of warm blood for transfusions, and cross-matching at body temperature; protection against cold after discharge from hospital; and regular checking of the blood count.

*J. M. Alexander*

**706. Atypical Pneumonia Treated with Streptomycin: a Preliminary Report on the Effectiveness of Streptomycin in Atypical Pneumonia**

F. P. KING. *Annals of Internal Medicine* [Ann. intern. Med.] 34, 141-147, Jan., 1951. 5 figs., 5 refs.

The author has treated 10 cases of atypical pneumonia with streptomycin. The dose of the antibiotic was 2 g. daily in divided doses every 6 hours for 5 days. Five of the cases are described in detail; in each of them penicillin had been used for a variable period before beginning streptomycin. A prompt improvement in the clinical condition was observed, and the author considers that streptomycin is a specific form of treatment for atypical pneumonia.

*T. Anderson*

**707. A Comparative Study of Three Types of Treatment for Pneumonia. (Tre typer af pneumonibehandling (419 tilfælde))**

J. B. NIELSEN and T. SØTTRUP. *Nordisk Medicin* [Nord. Med.] 45, 585-591, April 18, 1951. Bibliography.

The authors review 419 cases of pneumonia treated in the Centralsygehus, Randers, in 1945, 1947, and during a 12-month period in 1949-50. During the first period treatment was with sulphonamides, during the next with a combination of sulphonamides and penicillin, and in the third with penicillin. Although these series cannot be considered strictly comparable, as they were not observed during the same period, the authors affirm that on clinical grounds they may be considered similar, and that they also showed corresponding seasonal variations. Assessing the results of treatment by case mortality, fall of temperature, and duration of treatment there does not appear to be a significant difference between the groups. Only the mortality of infants with primary pneumonia decreased progressively during the 5-year period; this is considered to be due to more energetic general measures. Sulphonamide treatment involves a risk of side-effects, and for that reason alone the treatment of choice is now penicillin only.

*W. G. Harding*

See also Section Radiology, Abstracts 522 and 525.

**708. Bronchogenic Carcinoma as a Differential Diagnostic Problem in Pulmonary Disease. II. Carcinoma Arising from Major Bronchi Complicated by Secondary Infection**

J. H. MOYER and A. J. ACKERMAN. *American Review of Tuberculosis* [Amer. Rev. Tuberc.] 63, 255-274, March, 1951. 13 figs., 8 refs.

This is the second of an important series of articles discussing the differential diagnosis of bronchogenic carcinoma; it deals specifically with the difficulties in diagnosis when secondary infection complicates the growth in major bronchi. The problems are discussed in six groups: (1) acute pneumonic lesions; (2) unresolved pneumonia; (3) parenchymal invasion by carcinoma simulating pneumonia; (4) tuberculosis combined with bronchogenic carcinoma; (5) pneumonitis secondary to bronchogenic carcinoma simulating cardiac failure with thrombo-embolic manifestations; and (6) bronchogenic carcinoma associated with cavitation.

Differentiation may not be easy, and all available methods of investigation must be applied; a negative finding in any one method is not of such importance as a positive finding. It is emphasized here, as elsewhere in the literature, that inflammation distal to endobronchial neoplasms usually responds to chemotherapy, but is prone to relapse on cessation of therapy. Bronchiectasis is said to occur distal to a neoplasm in 20% of cases, and therefore its demonstration does not exclude the possibility of neoplasm. Bronchoscopy may not demonstrate a neoplasm, since many endobronchial tumours are beyond the range of the instrument. Bronchography and tomography are useful methods of demonstration of the bronchial lumen and its relationship to adjacent pulmonary infiltration. Re-aeration of an atelectatic portion of the lung may be due to necrosis of an endobronchial tumour with re-establishment of patency of the bronchus. Radiological clearing of the lesion is therefore not necessarily in favour of a non-malignant process. Parenchymal invasion by carcinoma may modify the signs of bronchial obstruction: the lung volume is normal, resembling a pneumonic consolidation and not an atelectasis. Deterioration in the condition of an apparently stable chronic case of pulmonary tuberculosis may be due to the superimposition of a bronchial carcinoma.

The differentiation between cardiac failure with thrombo-embolic pulmonary manifestations and pneumonitis behind bronchogenic carcinoma is very difficult; the symptomatology, the signs, and the radiological appearances are identical. Cases of carcinoma may be first seen with cavitation already established, and the diagnosis from pulmonary tuberculosis and lung abscess must then be made. Tomography will show the thickness and irregularity of the cavity wall, the contraction of the bronchus, and the peribronchial infiltration when necrosis of tumour tissue has produced the cavity. When the cavity is due only to infection following bronchial obstruction the characteristic appearance may not be present. In most cases the radiological appearance of a thick-walled, irregularly shaped cavity is diagnostic.

*John Sumner*

## Digestive Disorders

709. **Familial Lipaemia. A New Form of Lipoidosis showing Increase in Neutral Fats Combined with Attacks of Acute Pancreatitis.** [In English] H. M. POULSEN. *Acta Medica Scandinavica [Acta med. scand.]* 138, 413-420, Nov. 10, 1950. 19 refs.

This report comes from the Department of Surgery of the Central Hospital, Silkeborg, Denmark, and describes 2 cases. The first, a girl of 7 years, had a 2-year history of recurrent abdominal pain and was admitted with acute pancreatitis, which was associated with slight liver enlargement. Subsequent investigation revealed a marked rise in blood lipid and neutral fat levels, and to a lesser degree in that of cholesterol, the ratio of cholesterol ester to free cholesterol being decreased. The sternal marrow showed numerous reticular cells loaded with lipid. This patient's elder brother had a similar illness between the ages of 4 and 10 years, the clinical and laboratory findings being similar except for splenic as well as liver enlargement. However, he also had an unexplained encephalitis and at that time a retinal lipaemia. Re-examination at the age of 22 years showed him to be well, the only abnormalities being slight enlargement of the spleen and a persistent lipaemia, though considerably less than that found at the age of 5 years.

The author considers this condition to be a form of lipoidosis. The pancreatitis remains unexplained. He suggests that among children suffering from recurrent abdominal pain and liver enlargement may be found similar cases. A low-fat diet is reported to be the only useful measure for the reduction of the blood fat level.

R. N. Johnston

710. **Some Experiences with Chlortrimeton in the Treatment of Duodenal Ulcer** N. H. ISAACSON, J. L. KELLEY, and B. BLADES. *Medical Annals of the District of Columbia [Med. Ann. Distr. Columbia]* 20, 63-70 and 118, Feb., 1951. 5 figs., 44 refs.

After discussing the role of histamine in the stimulation of gastric secretion in health and disease, the authors report the treatment of 5 cases of radiologically proven duodenal ulcer, refractory to diet and other medication, with the antihistaminic "chlortrimeton" in doses of 8 mg. 4 times a day (after meals and at bed time) for about 10 weeks, no other form of therapy being given. While taking chlortrimeton all the patients were able to lead a completely normal life, eat a normal diet, and smoke as much as they pleased. Complete relief of symptoms was obtained in all cases within a few days, with a marked fall in gastric acid values and healing of the ulcer in at least 3 cases. All the patients were followed up for 6 to 8 months, and although the authors admit that it would be presumptuous to draw any definite conclusions from a study of only 5 cases, they suggest

that their findings indicate the need for further study of the therapeutic use of antihistaminics in cases of peptic ulcer.

S. Karani

### 711. Bleeding Peptic Ulcer

D. A. FERGUSON and A. L. WYMAN. *Lancet [Lancet]* 1, 814-818, April 14, 1951. 4 refs.

To a general hospital between January, 1947, and October, 1949, 157 cases of bleeding peptic ulcer were admitted. The over-all mortality was 17.8%, but 46.5% of the patients were over 60 years old. As usual, mortality was greatest amongst males, especially elderly males with chronic gastric ulcer. The frequency of severe intercurrent disease or diseases in such aged patients who die of gastro-duodenal haemorrhage is stressed, over one-half of those who died being thus doubly afflicted. This combination contributed a quarter of the deaths, torrential haemorrhage a sixth of the deaths, and emergency operation another sixth. The fatality rate in 11 such cases was 36%, but severely ill patients tended to be chosen for operation.

J. Naish

### 712. Pulmonary Emphysema in Association with Certain Diseases, especially Peptic Ulcer. (Lungemfysem vid vissa sjukdomar, speciellt magssar)

M. HIRVONEN and M. PERTTILÄ. *Nordisk Medicin [Nord. Med.]* 45, 513-515, April 4, 1951. 3 refs.

The authors had observed that peptic ulcer was present in a large number of cases of pulmonary emphysema. This led to the belief that the diagnosis of emphysema was often wrongly made, and extensive clinical investigation was thereupon carried out in this field, controls being instituted at the same time in the Department of Morbid Anatomy at Helsinki.

Since pulmonary emphysema has always been thought to be a disorder due mostly to old age and has been found to be more frequent in men than in women, the authors classified their patients in 4 age groups each for men and women. Each group contained 500 patients. Certain clinical signs of the presence of pulmonary emphysema—position of lung-liver borderline, area of absolute cardiac dullness, character of percussion note, intensity of breath and heart sounds—were noted as well as the radiographic findings. Changes in at least two of these signs were required for a diagnosis of pulmonary emphysema. Tables are given showing the results of the investigations. It appears that twice as many men suffer from this complaint as women, and that the incidence of pulmonary emphysema is highest in the age group 41 to 60, when it is approximately equal in the two sexes.

The control material investigated in the Department of Morbid Anatomy was classified in the same way. The criteria for the diagnosis of pulmonary emphysema were: diminished elasticity of the lung tissue, changes

in the external aspect and condition of the lung, amount of air in the lung tissue as a result of possible emphysematous vesicles in the lungs. It is revealed by the tables that the anatomical and clinical findings correspond in all age groups of men. In women, however, a much higher percentage of emphysema in all age groups was found post mortem than had been discovered by clinical diagnosis. From this it is adduced that the proportion of women who are suffering from emphysema is hardly any lower than that of men. It was also shown that emphysema had not been diagnosed too frequently. Another table shows the result of investigations on 1,238 patients suffering from peptic ulcer, and the post-mortem findings in 359 of these cases. It appears that pulmonary emphysema occurs about 1½ to 2 times as often in patients suffering from peptic ulcer than in others. The incidence of pulmonary emphysema in patients suffering from cancer of the stomach is slightly less.

Investigations were also made in 379 cases of asthma and it was found not only that the percentage of emphysema was higher than in the groups mentioned above, but that there was scarcely any difference between the age groups and none as between the sexes. The authors conclude that whereas there is an easy explanation for the frequent occurrence of pulmonary emphysema in asthma, no reason could be discovered for the high rate of this complaint occurring simultaneously with peptic ulcer; they attribute it to a constitutional tendency towards both emphysema and peptic ulcer.

E. S. Fountain

**713. The Relation of the Adrenal Cortex to Peptic Ulcer.** (Beziehungen zwischen Ulkuskrankheit und Nebenniere)

L. BIRÓ and G. NAGY. *Gastroenterologia* [Gastroenterologia, Basel] 76, 169-194, 1950-51. 49 refs.

**714. Activation of Peptic Ulcer during Pituitary Adrenocorticotropic Hormone Therapy. Report of Three Cases**

G. A. SMYTH. *Journal of the American Medical Association* [J. Amer. med. Ass.] 145, 474-477, Feb. 17, 1951. 9 refs.

The first of the 3 patients described, a man of 55, had had a duodenal ulcer for many years, but had been free from symptoms for 9 years. He was treated for lupus erythematosus with pituitary adrenocorticotropic hormone (ACTH); 5 days after the beginning of treatment (375 mg. ACTH) perforation of the ulcer occurred. A delay in diagnosis, due to the relatively low temperature and the lack of leucocyte response in the presence of peritonitis, contributed to the death of the patient. The tendency of ACTH to mask diagnostic signs has been noted by other authors.

The second patient, a man of 52, had a long history of duodenal ulcer with several haemorrhages. Another of these occurred during treatment with ACTH for psoriasis. As there was an interval of only 6 months between the last period of ulcer symptoms and this haemorrhage the element of coincidence cannot be

ruled out. The third patient, a man of 33, had a gastric ulcer with symptoms on admission. These settled down with dietary treatment. After 2 days' ACTH treatment (400 mg.) for mycosis fungoïdes he had a perforation. ACTH was stopped and his ulcer symptoms subsided with the appropriate treatment. He was later given cortisone without any aggravation of the ulcer symptoms.

It has been found experimentally that ACTH increases the excretion of uropepsin, which is considered to reflect the peptic activity of the stomach. It is also known that ACTH depresses the formation of granulation tissue in experimental wounds. These two factors probably have a bearing on the activation of peptic ulcers during ACTH administration.

Marianna Clark

**715. The Variable Effect of Atropine Sulfate on Fasting Gastric Secretion in Man**

E. LEVIN, J. B. KIRSNER, and W. L. PALMER. *Journal of Laboratory and Clinical Medicine* [J. Lab. clin. Med.] 37, 415-424, March, 1951. 3 figs., 23 refs.

The effect of intramuscular atropine in single doses of 1 and 2 mg., and also when repeated 4-hourly, has been studied on 35 subjects, most of whom had duodenal ulcers. After single doses, fewer than one-third showed any real reduction in either volume or acidity of the gastric secretion. When this occurred it was usually accompanied by toxic effects. Repeated injections also produced a variable response, increased secretion being noted in some cases. There was a tendency for the volume to be reduced more than 25% in about half the group, with less frequent reduction in free hydrochloric acid or total acidity. Toxic symptoms also accompanied this reduction frequently. The effect of atropine appears to be variable, unpredictable, and dependent on the subject's sensitivity as much as on the size of the dose.

Some of the literature is reviewed and factors producing the conflicting results are mentioned.

K. Gurling

**716. Quantitative Studies on the Mechanism of Gastric Secretion in Health and Disease**

L. R. DRAGSTEDT, E. R. WOODWARD, E. H. STORER, H. A. OBERHELMAN, and C. A. SMITH. *Annals of Surgery* [Ann. Surg.] 132, 626-640, Oct., 1950. 11 figs., 23 refs.

A singularly comprehensive series of animal experiments was performed to establish the relative amounts of hydrochloric acid poured out during the cephalic, gastric, and intestinal phases of gastric secretion.

Vagal denervation of the whole isolated stomach in a dog reduced acid secretion by an average of 76%, and crushing of the nerves produced a similar effect which has lasted over 2 years. Removal of the whole antrum reduced secretion from a Pavlov pouch by 86%, though excision of fractions of the antrum had no effect. Antral exclusion, as in the Finsterer operation (condemned by Ogilvie and others), produced variable results, perhaps owing to regurgitation of duodenal contents through the pylorus. Exteriorization of the antrum, however, was nearly as effective as its resection, and replacement

of the antrum in its normal position caused a return of acid secretion to previous levels, even though the antrum must now have lost the bulk of its nerve supply. Transplantation of the antrum as a diverticulum into the colon caused persistent hypersecretion of acid from the Pavlov pouch, though similar transplantation of part of the fundus had no effect. The antrum therefore appears to have a specific and powerful function in the production of gastric acid secretion, but only when in communication with the gut.

In normal dogs the nerve mechanism accounts for 45% of the 24-hour acid secretion, the antral hormone for another 45%, and the intestinal phase 10%.

Patients with duodenal ulcer secrete 3 or 4 times as much acid during the night as normal people, and about twice as much in response to histamine or insulin injection. In such patients probably 80% of gastric secretion is neurogenic, 15% promoted by an antral hormone, and 5% attributable to the intestinal phase. After complete vagotomy, both resting secretion and response to histamine are reduced by four-fifths.

H. Daintree Johnson

717. "Acid Phosphatases" in Fasting Stomach Secretion, with Special Reference to Cancer of the Stomach. ("Sure fosfataser" i fastende ventrikelsekret med henblik på diagnosen af cancer ventriculi) F. RØNNIKE. *Nordisk Medicin [Nord. Med.]* 45, 512-513, April 4, 1951. 2 refs.

The author, recognizing that early diagnosis of cancer of the stomach is of primary importance for the prognosis of this disease, has followed up previous work (Changus and Dunlop, *J. nat. Cancer Inst.*, 1949, 10, 481) on this subject and carried out the determination of acid phosphatase in the fasting stomach secretion. The tests were carried out at the Horsens Borough Hospital on 35 patients, of whom 10 were known to be suffering from cancer of the stomach (confirmed by either microscopy or laparotomy). X-ray examination failed to reveal any evidence of cancer in the remaining 25 patients.

Previous workers have considered that a finding in excess of 10 units of phosphatase per 100 ml. of fasting stomach secretion might indicate a diagnosis of cancer of the stomach at a stage when x-ray findings were still negative. The present author adopts the following criteria: pH not less than 3.5, since phosphatase activity decreases greatly at lower pH values; aspirated quantity not less than 10 ml., because a lesser amount was not considered to be a true sample of the stomach contents; storage at room temperature not to exceed 2 hours, or in a refrigerator 48 hours (phosphatase loses 7% of its activity after 24 hours at 4°C., and 70% after 24 hours at 21° to 26°C.); no significant admixture of blood or bile, owing to the fact that their presence raises the relative values.

Of the 35 cases tested, 9 are not reported upon. Of these 9, the pH in 8 was less than 3.5; in the one remaining, the results obtained from samples taken on two consecutive days varied greatly. Of the other 26 patients, 7 were suffering from cancer of the stomach. Of these there were 6 in whom phosphatase values above 10

units per 100 ml. were found. In the seventh patient the value was 6. Of 19 patients in whom no signs of cancer of the stomach had been detected, 18 had phosphatase values in excess of 10 units per 100 ml.

No definite correlation between pH and phosphatase values was found. A high pH, for instance, could yield either very high or very low phosphatase values in patients both with and without cancer. Moreover, no correlation was found between acidity, as determined by Ewald's test-meal, and phosphatase value. (Almost all the patients were achyllic.) The conclusion reached by the author is that the method under review is unsuitable for the early detection of cancer of the stomach.

E. S. Fountain

718. Relations between Histological Lesions and Radiological Signs in Cancer of the Gastric Mucosa. (Rapports entre les lésions histologiques et les signes radiologiques des cancers de la muqueuse gastrique)

G. ALBOT and J. TOULET. *Archives des Maladies de l'Appareil Digestif [Arch. Mal. Appar. dig.]* 40, 5-43, Jan., 1951. 34 figs., 15 refs.

Gastric carcinoma can often be diagnosed radiologically while the growth is limited to the glandular mucosa and before the muscularis mucosae is invaded. At this stage the surgeon is usually unable to palpate the lesion at laparotomy and the pathologist may find it difficult to pick out the suspicious area in the gastrectomy specimen. Comparison of the radiological and histological appearances permits a rational explanation of this paradox. Neoplastic cells produce a defence reaction. Even a small button of carcinoma may cause oedema and an inflammatory exudate. The important thing for the radiologist to remember is that the muscularis mucosae beneath the lesion may contract so that a stellate pattern of converging mucosal folds is produced, even though there be no ulcer or erosion. This contraction produces a localized area of rigidity which stretches less than the healthy surrounding wall when the stomach is filled with barium. A flat filling defect is produced, which in profile gives the "encastré" appearance. The depressed area, which is slightly overlapped by healthy stomach, resembles the socket which is cut to receive an inlay. [The word "encastré" (which seems to be finding its way into world literature) is equivalent to the English word "chased" in the expression "chased with precious stones".] In other cases the contraction of the muscularis mucosae is limited to the periphery of the neoplastic plaque and forms a ring which buckles the plaque outwards in a smooth arc. This is often wrongly interpreted as a superficial ulcer. These abnormal appearances may be seen only when the irritability of the gastric wall is increased by intravenous morphine or insulin. Early carcinoma will never be diagnosed where there is a waiting list for barium-meal examinations and the radiologist is always seeing irregularities due to ulcers which have healed by the time the patient comes for examination. The radiologist should insist on following up suspicious appearances, and this is impracticable if the proportion of indefinite cases is high. Clinical improvement and a negative gastroscopy, or even a negative

laparotomy, do not prove that radiological suspicions are unjustified. Occasionally a radiologist must insist on a partial gastrectomy even though clinician and surgeon refuse to take any responsibility for the diagnosis of a lesion.

[This paper is excellently illustrated and the reader is also referred to the 277 cases of early gastric carcinoma described by Toulet in his doctorate thesis (Paris, 1951). Barium-meal work in a few French clinics reaches a high standard and this paper emphasizes an important point. The x-ray silhouette of a gastric lesion depends mainly on functional changes in the muscularis mucosae and in the blood supply. The dehydrated, fixed laboratory specimen gives a misleading impression of the condition during life.]

Denys Jennings

See also *Abstracts of World Surgery*, 1951, 10, 73.

**719. Hepatic Lesions and Dysfunction associated with Chronic Ulcerative Colitis**

G. W. JONES, A. H. BAGGENSTOSS, and J. A. BARGEN. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] 221, 279-286, March, 1951. 3 figs., 15 refs.

From the Mayo Clinic comes this account of the investigation of the state of the liver in 91 cases of ulcerative colitis, examined post mortem: 90 consecutive necropsies in cases without colitis were taken as controls. The cases of ulcerative colitis were examined between 1936 and 1949. Mild fatty change was found in 12% of the controls and in 14% of the cases of ulcerative colitis; moderate fatty change in 5% of the controls and in 15% of ulcerative colitis cases; severe changes were present in 3% of the controls and in 37% of the ulcerative colitis cases. Cirrhosis was found in 3 cases of ulcerative colitis, and this and severe fatty change was found only in fulminating cases of ulcerative colitis with a reduced serum protein level, which they consider to be more probably the result of the colitis than of impaired liver function.

G. S. Crockett

See also Section Physiology and Biochemistry, Abstract 465.

**720. Pathological Liver with Minimal or no Change in "Liver Tests"**

W. E. RICKETTS. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] 221, 287-292, March, 1951. 4 figs., 4 refs.

In a number of cases of various types of liver disease, proved by needle biopsy or at laparotomy, a battery of 10 biochemical tests were carried out. These tests were found to be normal or to show only slight and usually inconstant variations from the normal in metastatic carcinoma, primary hepatoma, follicular lymphoma, calcified hydatid disease, sarcoidosis, histoplasmosis, Gaucher's disease, fatty infiltration, and amyloidosis. One-tenth of the normal parenchyma can carry on adequate function. The best single test is the bromsulphalein retention test to detect mild degrees of impairment.

G. S. Crockett

**721. A Study of Disorders of Capillary Permeability in Liver Disease. (Étude des troubles de la perméabilité capillaire en pathologie hépatique)**

R. CACHERA and F. DARNIS. *Archives des Maladies de l'Appareil Digestif* [Arch. Mal. Appar. dig.] 39, 1221-1245, Dec., 1950. 6 figs., bibliography.

The authors have studied the changes in capillary permeability and variations of fluid balance in 31 cases of disease of the liver. The capillary permeability was measured by: (1) Landis's test, which allows measurement of the water loss and protein leakage through the capillary walls in the upper arm during a known degree of venous compression; (2) the study of the rate of disappearance of Chicago 6B blue from the plasma before venous compression of the arm, and its concentration rate during venous compression. The extracellular fluid volumes were measured by both the sodium thiocyanate and Chicago-6B-blue tests. The results so obtained, together with the haematocrit values, allowed the calculation of the volume of extracellular fluids derived from the plasma, the total blood volume, and the interstitial fluid volume. A detailed account of these techniques is given in another paper.

From the above tests, repeated in the 31 cases at various stages of their disease, the authors conclude that the great loss of proteins which occurs in these cases compared with the comparatively small loss in normal subjects is very suggestive of primary alteration of capillary permeability. They consider that the change in the albumin-globulin ratio and the resultant lowering of the osmotic pressure of the blood are not alone enough to cause such outpouring of fluid into the tissues. Landis's test showed that the capillary permeability returns to normal very quickly in cases of infective hepatitis, and the results are paralleled by those obtained in routine liver function tests. After alcoholic hepatitis the capillary permeability takes many months to return to normal, and in cirrhosis (where the change in permeability is greatest) it may never do so. In obstructive jaundice the change in capillary permeability is very slight, but if the jaundice is accompanied by hepatitis then the changes are similar to those in the other liver diseases.

René Méndez

**722. Effect of Portal Cirrhosis on the Development of Carcinomas**

J. W. HALL and SHAO-CHIEN. *Cancer* [Cancer] 57, 131-135, Jan., 1951. 25 refs.

**723. Portal Cirrhosis: an Analysis of 208 Cases, with Correlation of Clinical, Laboratory and Autopsy Findings**

R. ARMAS-CRUZ, R. YAZIGI, O. LOPEZ, E. MONTERO, J. CABELO, and G. LOBO. *Gastroenterology* [Gastroenterology] 17, 327-343, March, 1951. 15 refs.

**724. The Clinical Value of Needle Biopsy of the Liver**

L. SCHIFF. *Annals of Internal Medicine* [Ann. intern. Med.] 34, 948-967, April, 1951. 12 figs., 19 refs.

# Endocrine Disorders

725. **Amenorrhoea in Anorexia Nervosa. Clinical, Biological, and Biochemical Aspects.** (L'aménorrhée des anorexies mentales; notions cliniques, étude biologique et biochimique)

J. DECOURT, M. F. JAYLE, G. H. LAVERGNE, and J. P. MICHAUD. *Annales d'Endocrinologie [Ann. Endocrinol., Paris]* 11, 571-592, 1950. 34 refs.

A clinical study has been made of 32 cases of anorexia nervosa with amenorrhoea. It was clear that the amenorrhoea often appeared early in the condition, indicating that it was a neuro-endocrine effect in the first instance rather than the result of malnutrition. In many cases psychiatric treatment, if sufficiently prolonged, was successful in re-establishing the menses and the return to normal weight of the patient; in other cases hormone therapy was necessary.

Laboratory investigation was carried out in 15 of the patients. Both the vaginal cytology and the output of urinary steroids showed a deficiency of oestrogens and progesterone as a result of ovarian insufficiency, the output of female sex hormones being normal in all but 2 patients.

In some cases the menstrual flow had been interrupted by a violent emotional shock and later the amenorrhoea-anorexia-emaciation syndrome had set in. Hence sympathetic stimulation was the primary cause and the endocrine disturbance was a secondary factor. The fact that the 17-ketosteroid output was normal or even raised indicated that there was adequate secretion of adrenocorticotrophic hormone and that hypophyseal failure was not responsible for the condition. However, in cases where the amenorrhoea and emaciation had lasted for many years the malnutrition had aggravated the endocrine insufficiency and led to pituitary dysfunction, so that the clinical picture was identical with that of Simmonds's disease. The success of psychiatric treatment in long-standing cases, however, indicated the psychic origin of the disease.

Nancy Gough

## EXPERIMENTAL ENDOCRINOLOGY

726. **Effect of Antihistamine Drugs on the Adrenal Cortical Response to Histamine and to Stress.**

J. TEPPERMAN, N. RAKIETEN, J. H. BIRNIE, and H. F. DIERMEIER. *Journal of Pharmacology and Experimental Therapeutics [J. Pharmacol.]* 101, 144-152, Feb., 1951. 5 figs., 16 refs.

The authors sought to discover whether the activation of the pituitary-adrenal system produced by the injection of histamine could be blocked by pre-treatment with antihistamine drugs. The experiment was performed on 200 adult albino rats with a mean weight of 240 g. The antihistamine drugs were tripeleannamine, diphenhydramine, and "phenoxydine" in doses that were approxi-

mately equimolar (30, 30, and 50 mg. per kg. of body weight respectively). The amount of ACTH released was estimated indirectly by the renal ascorbic acid depletion technique. An intraperitoneal injection of histamine phosphate in a dosage of 10 mg. per kg. of body weight produced a significant fall in adrenal ascorbic acid content. A diminution of this response was achieved by previous treatment with phenoxydine.

In a further experiment with the photo-electric tensiometer technique for studying blood-pressure responses in unanaesthetized rats, phenoxydine was shown to prevent the hypotensive action of histamine when given one hour before administration of the histamine in a dose of 50 mg. per kg. When the dose of histamine was increased to 100 mg. per kg. it was found that not even the highest dose of phenoxydine would prevent the fall in blood pressure.

These experiments were repeated with the other two drugs. It was established that the administration of these antihistamine drugs did not in itself cause any significant change in adrenal ascorbic acid content in the rat, whereas histamine reduced it from 400 mg. per 100 kg. to 277 mg. per 100 kg. of tissue. Histamine injection one hour after pre-treatment with phenoxydine or tripeleannamine resulted in a smaller fall in adrenal ascorbic acid content than in controls. Pre-treatment with diphenhydramine, however, did not modify the response to histamine injection, nor did pre-treatment with any of the antihistamine drugs prevent the reduction in adrenal ascorbic acid content in response to an intraperitoneal injection of carbon tetrachloride.

R. Hodgkinson

727. **The Influence of Age, Sex, and Weight on the Daily Excretion of 17-Ketosteroids in Normal Subjects.** (L'influenza dell'età, del sesso e del peso sulla eliminazione giornaliera dei 17-chetosteroidi nei soggetti normali)

A. CIOFFARI and E. COSSANDI. *Folia Endocrinologica, Pisa [Folia endocrinol., Pisa]* 3, 637-653, Aug., 1950. 4 figs., 18 refs.

The 17-ketosteroids in a 24-hour specimen of urine were estimated in 140 normal people (77 males and 63 females) ranging from 18 months to 80 years of age; the patient being weighed at the same time. The distribution of the subjects over the 5-year age groups was fairly even from 1 to 80 years, the age groups up to 30 containing the larger number (75) of cases.

[This is a considerable feat, considering the difficulty of collecting a 24-hour sample of urine in children up to 10 (31 cases).]

The conclusions are as follows. (1) The daily 17-ketosteroid excretion in the urine is influenced by age, being greatest between 20 and 40 years (12.5 mg.); after the age of 40 a gradual decline ensues to 7.5 mg. at 80. During the first 5 years of life it is very low (0.25 mg.), increasing to about 5 mg. at 10 years, and to 10 mg. at

15 years of age. (2) During the period of full sexual maturity, but especially between 20 and 40, men excrete considerably more than women; beyond 65 both sexes show a similar excretion (on a declining scale), provided their weight is equal; before puberty, there is no real difference between the sexes. (3) Body weight seems to have some [slight] influence on the daily excretion.

V. C. Medvei

**728. Dynamic Aspects of Sodium Metabolism in Experimental Adrenal Insufficiency using Radioactive Sodium**

T. N. STERN, V. V. COLE, A. C. BASS, and R. R. OVERMAN. *American Journal of Physiology [Amer. J. Physiol.]* 164, 437-449, Feb., 1951. 3 figs., 28 refs.

Although the concentration of sodium and chloride in the extracellular fluid was found to be decreased in dogs suffering from acute adrenal insufficiency, no evidence of an increase in the sodium of liver, spleen, heart, skeletal muscle, brain, bone, skin, or gut was obtained. The chloride concentration in muscle, heart, and brain was found to be increased. With  $^{24}\text{Na}$  no significant difference was found in the sodium turnover of erythrocytes in normal dogs and in animals with acute adrenal insufficiency, nor were the values for liver, muscle, heart, gut, and skin different in the two series of animals. However, some change in sodium metabolism of bone in animals with adrenal insufficiency was noted.

A. Schweitzer

**THYROID GLANDS**

**729. The Effect on Endogenous Thyroid Activity of Feeding Desiccated Thyroid to Normal Human Subjects**

M. A. GREER. *New England Journal of Medicine [New Engl. J. Med.]* 244, 385-390, March 15, 1951. 5 figs., 9 refs.

The depression of thyroid function by treatment with thyroid extract was measured in 47 human volunteers. In the first group 12 subjects were given 3 gr. (0.2 g.) of thyroid daily by mouth and all but one showed a marked depression of iodine uptake within 8 days. In the second group 25 subjects were given 1, 2, 3, and 4 gr. (0.06, 0.13, 0.2, and 0.26 g.) of thyroid for periods of 3 weeks at each level. One-third showed marked depression with 1 gr.; all but 4 with 2 gr.; all but 2 with 3 gr.; and all with 4 gr.

In another group recovery of thyroid function was studied after cessation of treatment. It occurred within 2 weeks in most instances, but 4 subjects still showed marked depression after 3 weeks, 2 after 6 weeks, and 1 after 11 weeks. Four apparently euthyroid subjects who had been taking thyroid for from 4 to 5 years also showed a similarly rapid rate of recovery after cessation of treatment.

Finally, 5 normal subjects were given 280  $\mu\text{g}$ . of iodine daily for 8 days and showed no fall, or only a slight fall, in iodine uptake. It is argued that the reduction in endogenous thyroid function is brought about by a depression of pituitary thyrotrophin secretion.

A. C. Crooke

**730. First Clinical Experiences with a New Antithyroid Drug: 6-Phenylthiouracil.** (Prime esperienze cliniche con un nuovo farmaco antitiroideo: il 6-fenil-tiouracile)

P. DEL MASCHIO. *Folia Endocrinologica, Pisa [Folia endocrinol., Pisa]* 3, 743-756, Oct., 1950. 27 refs.

The use of 6-phenylthiouracil in 20 patients with hyperthyroidism (17 women and 3 men) between 18 and 56 years of age is reported. In all cases there was improvement of the condition without any untoward effects. The most important point is that unusually high doses can be administered for a short time (1.0 to 1.5 g. daily); this is particularly useful in the case of preoperative treatment. The average dose used was 0.6 to 1.0 g. daily. Five patients were operated upon with good results. In one of them, friability and bleeding of the thyroid were noted during operation.

[The treatment did not, however, exceed 60 days, and was in most cases shorter than that. The recurrence rate is not mentioned, and no real evidence of permanent cure is given.]

V. C. Medvei

**731. The Nature of the Circulating Thyroid Hormone in Graves' Disease**

I. N. ROSENBERG. *Journal of Clinical Investigation [J. clin. Invest.]* 30, 1-10, Jan., 1951. 2 figs., 34 refs.

Careful plasma studies of 6 hyperthyroid patients 2 to 10 days after therapeutic doses (10 to 15 millicuries each) of carrier-free, radioactive sodium iodide ( $^{131}\text{I}$ ) had been administered indicated that up to 99% of the labelled iodine was protein-bound. Almost all of this labelled organic iodine in the plasma existed as a single substance, indistinguishable from thyroxine. The results of the study seem to show that the circulating hormone in Graves's disease is thyroxine. Monoiodotyrosine, diiodotyrosine, and acetylthyroxine were not found as constituents of the plasma protein-bound iodine.

[The technique for the quantitative extraction from plasma of the labelled protein-bound iodine should be studied in the original. This is a very important paper, because it provides proof that diiodotyrosine has no more effect and scope in the treatment of Graves's disease than Lugol's solution.]

V. C. Medvei

**ADRENAL GLANDS**

**732. Two Cases of Adrenal Hyperplasia with Adrenal Cortical Insufficiency**

N. E. FRANCE and C. A. NEILL. *Archives of Disease in Childhood [Arch. Dis. Childh.]* 26, 32-61, Feb., 1951. 8 figs., 27 refs.

The authors report 2 cases of the adrenogenital syndrome. Both were in female pseudo-hermaphrodites who developed typical symptoms of adrenocortical insufficiency after the first week of life. These symptoms were: insidious onset of vomiting, with passage of small, loose stools and mucus, lethargy, anorexia, pyrexia, and sweating; sudden crises occurred, Addisonian in type, with dehydration, collapse, and contracted pupils.

In one case the condition was diagnosed while the patient was alive, and in the other at necropsy.

The internal genitalia showed only slight variations from those of the normal female; bilateral hyperplasia of the adrenals with thickening of the cortex was present (combined weights being 11.5 g. and 13 g. respectively). In neither case was there family history of abnormality.

The first patient was normal until the 7th day, except for abnormal external genitalia. The serum electrolyte levels were normal on the 6th day, but with the occurrence of crises on the 18th, 30th, 41st, and 53rd days an imbalance appeared (low serum sodium and chloride, and high serum potassium and urinary chloride levels). The diagnostic value of biochemical examinations is stressed. Improvement followed administration of saline (up to 2 g. salt a day); this regimen was maintained during life (57 days), with "eucortone" during crises. After the fourth crisis, eucortone, 5 ml. 4-hourly, and saline intravenously were given without success. The adrenal cortex showed, microscopically, deficiency of the glomerular zone, a normal fascicular zone, and a thick reticular layer containing cells of both adult and foetal type. In the second infant, considered to be a male child with hypospadias during life (261 days), the condition followed a longer and less acute course. Crises were treated empirically with saline. Remissions occurred and death was unexpectedly sudden. Here the glomerular zone of the cortex was more prominent, the fascicular zone almost absent, and the reticular layer thickened but without cells of foetal type.

The glomerular zone being regarded as the source of electrolyte-and-water-control hormone, a relationship is suggested between the histological and clinical findings in the 2 cases. At present no inhibitory treatment is known against the production of androgens, possibly by both foetal and adult types of cell, in the zona reticularis.

V. Reade

### 733. The Effects of Adrenocorticotropic Hormone and Cortisone in the Adrenogenital Syndrome Associated with Congenital Adrenal Hyperplasia: an Attempt to Explain and Correct its Disordered Hormonal Pattern

F. C. BARTTER, F. ALBRIGHT, A. P. FORBES, A. LEAF, E. DEMPSEY, and E. CARROLL. *Journal of Clinical Investigation* [J. clin. Invest.] 30, 237-251, March, 1951. 13 figs., 25 refs.

This paper from the Massachusetts General Hospital describes detailed metabolic studies on 3 female children suffering from the adrenogenital syndrome. In many respects these patients showed an abnormal response following the administration of ACTH. There was no significant increase of urinary 11-oxysteroids, and the patients did not develop a negative nitrogen balance or show a reduction of circulating eosinophils. There was also a failure to develop sodium and chloride retention. The urinary 17-ketosteroid content, however, definitely rose. These findings suggested that in this syndrome the adrenal cortex is unable to respond normally to ACTH by increased production of "carbohydrate-active" and "salt-retaining" steroids, but that it is capable of a response by producing androgens.

Administration of cortisone acetate (100 mg. daily for 12 days) to 2 patients produced a markedly negative nitrogen balance and a fall of urinary 17-ketosteroid level to normal. The authors suggest that the action of cortisone on the 17-ketosteroid excretion was due to depression of pituitary ACTH production. It is postulated that the adrenal androgens inhibit ACTH production relatively weakly, whereas "sugar hormone" inhibits ACTH production relatively strongly. If then the adrenal production of sugar hormone is deficient, pituitary ACTH production is not depressed and more ACTH is secreted. This in turn leads to an over-production of adrenal androgen. Both these patients were subsequently given a prolonged course of cortisone (50 to 100 mg. twice weekly). At the time of writing (6 months) the urinary ketosteroids had been maintained at normal levels, but it was too early to decide whether further virilism could be prevented by this therapy.

G. Ansell

### 734. Results of Cortisone Treatment in Dublin

MEDICAL RESEARCH COUNCIL OF IRELAND. *Irish Journal of Medical Science* [Irish J. med. Sci.] 6, 95-113, March, 1951.

In this preliminary report on the clinical investigation of cortisone by the Medical Research Council of Ireland, 15 cases of rheumatoid arthritis are described. The usual intramuscular dose of cortisone was about 100 mg., although double this dosage was often employed for a few days. The maximum degree of remission occurred in 2 to 6 weeks. A course at full dosage lasted 3 to 6 weeks and the total dosage did not exceed 6 g. A difficulty was to know how to treat cases which relapsed in a week or two after a full course and required the hormone for long periods 2 to 4 times a week to keep the arthritis under control, especially when side-effects appeared. The best results were obtained in those cases treated before destructive lesions in the joints were sufficient to cause extensive damage to cartilage or bone. The estimation of functional improvement varied from between 70 to 85%. In all cases, however, relapse was expected sooner or later and then cortisone treatment was to be resumed.

For ophthalmic work subconjunctival injection was decided upon as the method most likely to give maximum local concentration with the least danger of causing any general upset. A dose of 0.05 ml. containing 1.25 mg. of cortisone, was given subconjunctivally under surface analgesia produced by 2% cocaine. There was little irritation. The material remained visible as a gradually decreasing deposit for 5 or 6 days, at the end of which time a second injection was given. Five types of case were considered suitable for cortisone therapy. In the first group of ocular complications of rheumatoid arthritis certain cases treated by the authors cleared with rapidity. The second group, of conditions of the anterior segment in which bacteria were not the cause, such as interstitial keratitis, responded very satisfactorily. Other types of keratitis improved in about 60% of cases. In 3 cases of iridocyclitis there was some improvement. In the third group, consisting of healing corneal inflammations or burns (3 cases of

severe corneal opacities following lime and acid burns), clearing of the corneal opacity was accelerated and increased. In the fourth group no improvement was recorded in one case of vascular degeneration of the posterior segment. In the fifth group, consisting of allergic cases, no cases were treated. In 34 cases cortisone eye drops and ointment were used in addition to subconjunctival injection. It is pointed out that many ocular conditions, such as interstitial keratitis, uveitis, and phlyctenular conjunctivitis, are due to reactions in the eye produced by stress in other parts of the body.

In 8 cases of toxæmia of pregnancy clinical improvement occurred out of all proportion to the changes in the blood pressure, albuminuria, and oedema. The oedema, however, frequently improved remarkably, while the effect on the blood pressure and albuminuria varied, with a tendency to fall. It was the authors' opinion that the patients became less liable to develop fits.

In general it was considered that cortisone had its greatest use in diseases of limited duration such as rheumatic fever, toxæmia of pregnancy, ophthalmic diseases, and some allergic conditions. The effect of cortisone had been studied on 142 patients up to February, 1951 (most of whom are not included in this preliminary report) including 88 eye cases, 29 cases of arthritis, 4 cases of rheumatic fever, and 8 cases of toxæmia of pregnancy. An account of the physiological background of cortisone is included in this article.

R. Hodgkinson

### 735. The Adrenogenital Syndrome in Childhood. (Síndrome adreno-genital na infância)

A. Z. FLOSI. *Revista do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo* [Rev. Hosp. Clin. Univ. S. Paulo] 5, 226-254, Oct., 1950. 21 figs., bibliography.

The clinical history is given, with photographs, of 4 cases of the adrenogenital syndrome in infants, 1 being 4 years old and the other 3 under 2 years; 3 were girls. The most significant changes were that they were too tall for their age, their muscular system was overdeveloped, the clitoris or penis enlarged, pubic and peri-anal hair was present (none had axillary hair), and one of the girls had a beard; 3 of the patients had a palpable adrenal tumour and one an enlarged liver, probably due to secondary deposits. All showed an excessive excretion of 17-ketosteroids, and x-ray examination in 3 of the cases showed centres of ossification of an older age group. The diagnosis was confirmed in 3 cases at necropsy: 2 died of acute adrenal failure immediately after operation.

Most of the cases of adrenogenital syndrome in infancy are due to malignant adrenal tumours which metastasize to liver and lungs. The tumours contain cells closely resembling those of the reticular and fascicular zones, or they may be anaplastic. Haemorrhage may occur, to be followed by calcification. It would appear that androgenic activity, which is responsible for this syndrome, is mainly due to hyperfunction of the reticular zone. The hormones mainly

responsible are anabolic, resulting in nitrogen retention and build-up of protein. There is also a close relationship between androgenic activity and the excretion of the 17-ketosteroids.

Amongst the changes in the genital organs, it was noted that in the boy the testicles were small; this is the usual finding as both the Leydig and spermatogenic cells tend to remain atrophic. In one girl the clitoris was so large as to simulate a penis with hypospadias. This enlargement of the clitoris is an important diagnostic sign. In no case was there menstruation or enlargement of the breasts. The uterus, tubes, and ovaries remained infantile, and vaginal smears showed atrophic epithelium. The presence of an adrenal tumour may be diagnosed by palpation, plain x-ray examination, and intravenous pyelography or peri-renal insufflation of air, this last procedure being, of course, a dangerous one.

In boys the differential diagnosis is from a testicular tumour and the hypothalamic syndrome; the former is usually easily palpable, whereas in the latter there is an increase in gonadotrophins in the urine. In girls ovarian tumours and hypothalamic disturbances tend to produce homosexual changes, and there is little change in the 17-ketosteroid excretion. An increased excretion of the beta-17-ketosteroids indicates adrenal tumour (Talbot).

The prognosis is very bad and the treatment is essentially surgical. In one series only 14 out of 35 patients survived the operation, death being due to an adrenal crisis following removal of the tumour, the remaining gland being atrophic. The 2 patients subjected to operation died in spite of salt, glucose, and cortical extract freely administered.

Paul B. Woolley

### 736. Extract of Licorice for the Treatment of Addison's Disease

J. GROEN, H. PELSER, A. F. WILLEBRANDS, and C. E. KAMMINGA. *New England Journal of Medicine* [New Engl. J. Med.] 244, 471-475, March 29, 1951. 5 figs., 8 refs.

The case is reported of a patient with Addison's disease who improved clinically and biochemically when given 15 to 30 g. of liquorice extract daily and who relapsed when treatment was stopped. The observation confirms the finding of Borst *et al.* (*Acta clin. belg.*, 1950, 5, 405) that liquorice contains a substance with a deoxycortone-like action on oral administration.

A. C. Crooke

### 737. The Electrocardiogram in Addison's Disease

W. SOMERVILLE, H. D. LEVINE, and G. W. THORN. *Medicine* [Medicine, Baltimore] 30, 43-79, Feb., 1951. 13 figs., 27 refs.

The abnormalities of the electrocardiographic pattern encountered in a series of 90 patients with Addison's disease were thought to be due to numerous causes, notably deficiency of the adrenocortical carbohydrate-regulating factor, tissue electrolyte imbalance, changes in extracellular fluid volume, lowered basal metabolic

rate, and myocardial degenerative lesions. No single electrocardiographic pattern could be defined as typical of Addison's disease; indeed in 48% of this series the records were normal.

Whereas treatment with deoxycortone acetate in most cases caused no electrocardiographic change despite clinical improvement, it accentuated the electrocardiographic abnormalities in 22%, possibly because the improved circulation then unmasked latent myocardial damage. The authors also suggest that the fall produced in serum potassium level may be another factor. Necropsy findings in 5 cases are discussed; in 3 there were localized areas of myocardial necrosis with fibrous replacement.

J. L. Lovibond

## GENITAL GLANDS

### 738. Male Pseudohermaphroditism. A Type Showing Habitus, Absence of Uterus, and Male Gonads often Associated with Testicular Tubular Adenoma. Report of Case and Review of Literature

M. WACHSTEIN and A. SCORZA. *American Journal of Clinical Pathology* [Amer. J. clin. Path.] **21**, 10-23, Jan., 1951. 5 figs., 32 refs.

The authors believe that their case of male pseudohermaphroditism in a 20-year-old girl is an example of a definite clinical entity, and have collected 20 similar cases from the literature. The hereditary factor was shown by the fact that there were 3 pairs of sisters, and 3 cases with a history of primary amenorrhoea among sisters and aunts. All showed typical female sex characteristics and normal external genitalia, except for lack of pubic and axillary hair. The vagina was short and the uterus absent. In the majority of cases one or both gonads were found in the inguinal canal, and it was usually for the discomfort thus caused that advice was sought.

The histology of the gonads examined was that of immature testicles with marked hyperplasia of Leydig cells and testicular tubular adenoma in most instances. Hormone studies were incomplete, but the urinary excretion of 17-ketosteroids was mostly normal, that of oestrogen lowered, and of gonadotrophin raised.

D. W. Higson

### 739. New Criteria in the Differential Diagnosis between Primary and Hypopituitary Forms of Male Hypogonadism. (Nuovi criteri diagnostici differenziali tra forme primitive ed ipofisarie dell'ipogenitalismo maschile)

F. CERESA. *Minerva Medica* [Minerva med., Torino] **41**, 1095-1101, Nov. 24, 1950. 44 refs.

After discussing in detail previous attempts to distinguish between primary and hypopituitary male hypogonadism, the author describes his own investigations on 37 patients. His conclusions are: (1) In primary male hypogonadism (a) the excretion of gonad-stimulating hormone in the urine is normal; (b) the response to the gonadotrophin-stimulation test of Ceresa and Rubino (described in the same issue of *Minerva Medica*) is negative; (c) there is no response to treatment

with gonadotrophic hormone; (d) the excretion of 20-ketosteroids in the urine is normal. (2) In hypopituitary male hypogonadism (a) there is very little, if any, gonad-stimulating hormone in the urine; (b) the Ceresa and Rubino test is positive; (c) there is a response to treatment with gonadotrophic hormone; (d) the excretion of 20-ketosteroids in the urine is often diminished.

[This is an important piece of work; if the findings of the author are confirmed a difficult problem will have been solved.]

V. C. Medvei

### 740. Turner's Syndrome: Personal Observations in Five Cases. (Le syndrome de Turner. A propos de 5 observations personnelles)

M. ALBEAUX-FERNET, J. DERIBREUX, S. TCHEKOFF, and P. BREANT. *Presse Médicale* [Pr. méd.] **59**, 285-290, March 7, 1951. 6 figs., bibliography.

This paper gives a full description of 5 cases of Turner's syndrome, seen over a period of 3 years, in girls aged 15 to 18 years. All were of short nature, one being stocky in build but the others having normal proportions; the height ranged from 1.28 to 1.47 metres. A distinctly short neck was found in only 2 cases and cubitus valgus in only 1 case. Axillary and pubic hair was either absent or very scanty and the genital organs (including the breasts) were infantile in all cases. Only minor congenital anomalies, such as naevi, were present in 3 cases, none being detected in the others. In all cases, skiagrams showed unfused epiphyses of the long bones. Determination of follicle-stimulating hormone excretion showed high titres in 3 cases, but only questionably raised levels in the first 2 cases [in which an older, evidently less reliable, technique had been used]. Coelioscopy demonstrated the absence of recognizable ovaries in 4 cases, while in the fifth no left ovary could be seen and the right ovary was rudimentary. 17-Ketosteroid excretion was low in 2 cases out of 4, but within normal limits in the other 2.

In 2 cases craniotomy revealed localized, encysted, serous meningitic lesions which were drained. Following the operations some growth and sexual development occurred. Air encephalography (by the lumbar route) was performed in 2 of the remaining cases; in 1 the lateral ventricles appeared to be aplastic, with an enlarged basal cistern; in the other no abnormalities were found. Treatment in 3 of the cases with oestrogens produced the expected changes in sexual characters and provoked uterine bleeding.

The authors review all the previously reported cases and discuss at length the possible aetiology of the condition. They conclude that it arises through disturbances of embryonic development, perhaps mainly of infectious origin in the mother, and that these disturbances are more severe the earlier in embryonic life that they occur. They believe that the abnormally slow growth, absence or failure of development of the ovaries, and the other congenital anomalies seen are coexistent consequences of disordered embryogenesis rather than being in any way dependent one on another.

G. I. M. Swyer

## Dermatology

### 741. Evidence of Adreno-cortical Stimulation by Auto-hemotherapy

G. C. SAUER. *Journal of Investigative Dermatology* [J. invest. Derm.] 16, 177-192, March, 1951. 5 figs., bibliography.

Various theories have been propounded from time to time to explain the supposed beneficial effect of auto-haemotherapy in certain skin diseases such as, for example, psoriasis. The present author suggests that the procedure causes an alarm reaction in the general adaptation syndrome, resulting in mild stimulation of the adrenal cortex with consequent increased secretion of the 11- and 17-oxysteroid hormones.

Haematological changes following non-specific stress, and also the administration of ACTH, are stated to be: (1) an immediate decrease in the total leucocyte count followed by a more definite increase due to a neutrophil leucocytosis; (2) an initial rise in lymphocyte count followed by a fall; and (3) a fall in eosinophil count. The author selected the change in number of circulating eosinophils as the index for measuring the stimulating effect of autohaemotherapy on the adrenal cortex and carried out studies on 20 subjects. For controls he used adrenaline as a drug known to stimulate the adrenal cortex and saline as a substance which presumably has no such effect. The results showed that qualitatively the blood changes after autohaemotherapy and adrenaline were quite similar, a significant fall occurring in the number of circulating eosinophils and a rise in the absolute number of neutrophils. The saline injections did not bring about the same changes. (In the subsequent discussion one of the speakers suggested that seeing blood taken out of the arm and injected into the hip might be a factor in inducing psychological stress and an alarm reaction.)

E. W. Prosser Thomas

### 742. The Effects of Penicillin on Certain Hitherto Incurable Dermatoses

V. H. WITTEN. *Journal of Investigative Dermatology* [J. invest. Derm.] 16, 193-200, March, 1951. 4 refs.

During the past few years reports have been published on the beneficial effects of systemic penicillin in acrodermatitis chronica atrophicans (Hroxheimer) (for example, by Thyresson on 57 cases so treated in Stockholm). The present author confirms these good results in 6 cases, in which he obtained moderate to marked improvement in 4 cases, only slight improvement in 1 case, and no change in 1 case. As in previously recorded cases, the least satisfactory results occurred where atrophy was pronounced.

Systemic penicillin has also been reported of value in Kaposi's haemorrhagic sarcoma, but in 6 cases in which the author tried it there was no significant improvement.

E. W. Prosser Thomas

### 743. Recurrences after Vitamin-D<sub>2</sub> Treatment of Lupus Vulgaris. (Rückfälle nach der Vitamin-D<sub>2</sub>-Behandlung der Tuberculosis luposa)

W. BRAUN. *Hautarzt* [Hautarzt] 2, 72-76, Feb., 1951. 8 figs., 17 refs.

Of 12 patients with lupus vulgaris treated with vitamin D<sub>2</sub> for one year, 5 had clinical relapse 6 to 10 months after cessation of treatment. In all these cases the original therapy had been continued for at least 3 months after "clinical cure". It is concluded that treatment for one year with vitamin D<sub>2</sub> may not be adequate.

G. W. Csonka

### 744. Adrenocorticotropic Hormone (ACTH): its Effect in Atopic Dermatitis

T. G. RANDOLPH and J. P. ROLLINS. *Annals of Allergy* [Ann. Allergy] 9, 1-10, and 18, Jan.-Feb., 1951. 9 figs., 13 refs.

Four patients with atopic dermatitis, which was accentuated by known allergenic foods but had not responded well to specific treatment, received 6-hourly doses of 20 to 50 mg. ACTH for periods of 3 days in the first 3 cases and of 3 weeks in the fourth case. The patients' respective ages were 31, 6, 3½, and 6 years. A substantial clinical improvement was found after the first 24 hours of treatment and is evident in the photographs reproduced. In the 2 cases in which the incriminated foodstuffs were included in the diet symptoms recurred 4 and 5 days after cessation of treatment. In 2 cases in which they were avoided, they recurred after 2 and 10 days respectively.

H. Herxheimer

### 745. Effect of ACTH in Acute Dermatomyositis

M. M. SUZMAN and J. A. RUDOLPH. *Lancet* [Lancet] 1, 660-663, March 24, 1951. 1 fig., 4 refs.

After reviewing 7 cases described in the literature of dermatomyositis treated with ACTH with rather varying success, the authors report the effect of the drug on a man aged 38 who was critically ill with pyrexia, swollen joints, severe pains in the muscles of neck, shoulders, and limbs associated with wasting and widespread myasthenia. The patient's condition had rapidly deteriorated despite the administration of sulphonamides, aureomycin, penicillin, salicylates, pregnenolone, deoxycortone, and testosterone, each in combination with ascorbic acid. The patient had a history of rheumatic fever in childhood and had chronic valvular heart disease.

Dramatic improvement occurred on giving ACTH intramuscularly, the initial dosage being 10 mg. 6-hourly for 15 days, this later being reduced to 10 mg. daily and finally to 10 mg. once a week because of lack of supplies. The patient had recovered and could attend to his business after 860 mg. of ACTH had been given in 99 days. No relapse occurred during the 14 weeks after stopping

the drug. [The only skin manifestations, apparently, were redness over the left ankle and right wrist, a fine erythematous maculopapular rash on the back, and thickening and firmness of the skin. Sections of the skin and muscle suggested one of the group of collagen diseases, but no definite histological features of dermatomyositis were detected.] *E. W. Prosser Thomas*

**746. ACTH and Cortisone in Diffuse Collagen Disease and Chronic Dermatoses. Differential Therapeutic Effects**  
E. N. IRONS, J. P. AYER, R. G. BROWN, and S. H. ARMSTRONG. *Journal of the American Medical Association* [J. Amer. med. Ass.] 145, 861-869, March 24, 1951. 5 figs., 21 refs.

In the course of investigation and treatment of 13 patients it was observed that some affections not responsive to cortisone, such as psoriasis, exfoliative dermatitis, and scleroedema, were responsive to ACTH. In the collagenous diseases such as lupus erythematosus ACTH produced remissions more quickly than cortisone, but there was a high incidence of complications on long-term therapy. It was advantageous to start treatment with ACTH and then to substitute cortisone therapy. A salt-restricted diet and the administration of potassium were regarded as necessary, and the use of mercurial diuretics in patients with salt and water retention is discussed.

Permanent cure was not obtained in any of the cases treated, and one patient died. It is stressed that in cases where bacterial allergy may be an aetiological factor, treatment with antibiotics should be tried before employing ACTH or cortisone. There was not always a correlation between eosinophil response and clinical response to treatment.

*John T. Ingram*

**747. Systemic Lupus Erythematosus. Some Cutaneous Manifestations Related to the Diffuse Collagenous Diseases**

B. SHAFFER, G. W. JAMES, J. P. SCULLY, and D. M. PILLSBURY. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] 221, 314-318, March, 1951. 20 refs.

Three cases of systemic lupus erythematosus are described and discussed. The first was that of a woman of 25 who first developed the chronic discoid variety of the disease. This was followed by attacks of the acute disseminated variety and, on one occasion, by lesions of the profundus type. Other lesions appeared which closely resembled papulo-necrotic tuberculides, erythema nodosum, and periarthritis nodosa. There were multiple chronic foci of infection. Intracutaneous tests with very low concentrations of *Staphylococcus aureus haemolyticus*, *Streptococcus haemolyticus*, and *Strep. viridans* all showed marked sensitivity. The second patient, a woman of 38, had suffered from Raynaud's syndrome since the age of 16. She had evidence of old lung and kidney infections. Chronic discoid lupus erythematosus was followed by a scarlatiniform eruption attributed to taking sulphonamides. Later there appeared erythema nodosum, obliteration of the left ulnar artery, and fluffy exudates in the fundus of the left eye. The third patient, a woman of 27, had fulminating disseminated

lupus erythematosus. There were raised blood pressure, an erythematopapular rash, retinopathy, nephritis, adhesive pericarditis, endocarditis, and purpura. Post-mortem examination revealed marked degeneration of the adrenal glands.

All the conditions described are primarily vascular changes brought about by hyperergic reactivity to many antigens. Sunlight and sulphonamides may act as precipitating factors. The important role of the adrenal cortex in vascular physiology and the remissions which may result from cortisone therapy suggest that the vascular system is the fundamental site of this disease.

*E. Lipman Cohen*

**748. The Effect of ACTH on Psoriasis Arthropathica et Ungium. (Zur Wirkung des ACTH (Cortiphysen) auf die Psoriasis arthropathica et ungium)**  
K. W. KALKOFF. *Dermatologische Wochenschrift* [Derm. Wschr.] 123, 361-367, 1951. 4 figs., 12 refs.

After a short review of the literature the author presents 2 cases of psoriasis arthropathica et ungium. The first patient gave a history of psoriasis for 23 years, with involvement of the joints for 9 years and of the nails for one year; 67.5 mg. ACTH was given, with immediate improvement, and followed on the 22nd to 24th day by 90, 90, and 22.5 mg. ACTH respectively. All lesions responded well, but a recurrence of the skin and joint lesions occurred 8 months later. The latter in this case were acute, with periarticular oedema. The second patient had a similar history. She was given a course of ACTH (22.5 mg. 6-hourly, total 382 mg.) with a good clinical response, and 12 days later another course (90 mg. daily for 3 days, and then 22.5 mg. daily for 7 days). The skin lesions on the trunk healed, those on the arms improved, but no change was noted on the legs. This might be due to stasis in the thighs. The joint lesions, which were painless and chronic, remained unchanged.

In both cases the nails were cured and a distinct hyperkeratotic line of demarcation several millimetres in breadth divided the affected, discoloured, distal part of the nail from the healthy, recently grown, proximal part. This line of demarcation indicated the time at which the ACTH took effect. By measurement of the distance between this line and the eponychium this time could be calculated with a moderate degree of accuracy, showing that the effect of ACTH is much more instantaneous than that of other methods of treatment, where the transition from affected to healthy nail can hardly be demonstrated at all.

*Ferdinand Hillman*

**749. Recurrent Bullous Eruption of the Feet**

S. T. ANNING. *British Journal of Dermatology* [Brit. J. Derm.] 63, 104-110, March, 1951. 2 figs., 21 refs.

The literature on recurrent bullous eruption of the feet is reviewed and all cases reported are summarized. Two further families are described in which this condition was transmitted through both males and females as a dominant. In no family was there a case of epidermolysis bullosa simplex, and the author agrees with Haldane and Poole and Cockayne that recurrent bullous eruption of the feet is a clinical entity differing from other forms of epidermolysis bullosa.

*H. R. Vickers*

## Venereal Diseases

750. **Aureomycin and Chloramphenicol in Chancroid**  
R. R. WILLCOX. *British Medical Journal [Brit. med. J.]* 1, 509-510, March 10, 1951. 16 refs.

Bubo fluid from patients suffering from chancroid ulcer was found to be of high virulence on inoculation into volunteer recipients. The development of a chancroid ulcer by inoculation was prevented by instituting treatment with chloramphenicol or with aureomycin. Inoculation of bubo fluid collected from the patient after his treatment had been started with chloramphenicol or with aureomycin gave unsuccessful results.

The chancroid ulcer in 2 cases treated with chloramphenicol (250 mg. orally three times daily for 3 days) and in one case treated orally with aureomycin (2,000 mg. during 3 days) healed in 3 to 5 days. In one of these cases a bubo needed aspiration on the fourth day, but the aspirated fluid proved to be avirulent on inoculation.

V. E. Lloyd

751. **Terramycin in the Treatment of Gonorrhea in Women. [In English]**

T. PUTKONEN. *Annales Medicinae Experimentalis et Biologiae Fenniae [Ann. Med. exp. Biol. fenn.]* 29, 115-118, 1951. 5 refs.

The author treated 69 females suffering from gonorrhoea with single oral doses of terramycin. Patients were kept in hospital for 2 weeks, and regarded as cured if 4 negative post-treatment smears and cultures were obtained during this time. Only 6 of 12 patients were cured when given 0.5 g., but of 55 given 1 g., 45 (82%) were considered cured. It is concluded that terramycin is an effective drug in the treatment of gonorrhoea, although in the doses given the results were slightly inferior to those obtained with single injections of either penicillin or streptomycin. "It seems that terramycin will not supersede parenteral penicillin in the treatment of gonorrhoea, but it can compete with penicillin in those cases in which oral treatment is preferable."

[These results are considerably better than those obtained by the abstracter with single doses. They can be improved by giving two doses each of 1 g. at an interval of 6 hours.]

R. R. Willcox

### SYPHILIS

752. **Penicillin Treatment of Syphilis in Children. (Пенициллин в терапии сифилиса у детей)**

M. M. RAITZ, G. L. FABRIKANT, and I. S. LIBERMAN. *Pediatrija* No. 1, 35-40, 1951.

A group of 220 children with syphilis were treated with penicillin and observed over a period of up to 4 years; 130 were infants with congenital infection; one-third of the cases were not seen until the disease had been present for 1 to 3 months. The dose was 300,000 to

500,000 units per kg. daily in 6 doses given intramuscularly (latterly changed to 3 doses given subcutaneously) in 0.5% procaine; the course of treatment lasted for 12 to 15 days and was repeated after 3 to 4 weeks. Small doses (5,000 units) were given at first in order to avoid Herxheimer reactions, and the dose was increased later to 20,000 units. Skin lesions regressed in 3 to 10 days, and rhinitis disappeared in a quarter of the cases at the end of one course; destructive bone lesions healed after 1 to 2 months, and periostitis after 2 to 4 months. Enlargement of the liver and spleen responded less rapidly and often progressed during the course of treatment, but nephritis improved rapidly and the urine was often normal at the end of the first course. The general condition of the infants improved, anaemia disappeared, and they put on weight. Of 135 children, 76 of whom were infants with congenital syphilis, 15 died (13 infants), 10 of them during the first course, while 6 died out of 93 children (including 75 infants) treated subsequently with larger doses. The Wassermann reaction usually became negative 2 to 4 months after beginning treatment, but remained positive in some cases until combined therapy was given. Arsenical compounds were given at a later stage in view of the possibility of relapse after treatment with penicillin alone.

The authors also gave penicillin treatment to 40 patients between the ages of 6 and 17 years suffering from acquired syphilis. Smaller doses were given in this group; 100,000 to 150,000 units were given per kg., with a total of 2 to 3.5 million in a course. Good results were obtained; there was complete restoration of vision in 5 of 7 cases of keratitis, involvement of the central nervous system was arrested in other cases, and the Wassermann reaction became negative in 10 of 16 patients. Relapses may occur later if treatment with the usual preparations is not given as well.

D. J. Bauer

753. **Treatment of Neurosyphilis with Penicillin Combined with Artificial Fever Therapy. II. Further Observations**

N. N. EPSTEIN and J. R. ALLEN. *Archives of Dermatology and Syphilology [Arch. Derm. Syph., Chicago]* 63, 419-425, April, 1951. 5 refs.

Though excellent results in the treatment of neurosyphilis with penicillin alone have been reported by many workers, the authors are persisting in the study of the fever-with-penicillin method of therapy, believing that the ultimate efficacy of any treatment cannot be ascertained until after many years of study: 81 patients with various forms of neurosyphilis were treated with approximately 20 daily injections of 300,000 units of procaine penicillin in oil with aluminium monostearate (P.A.M.). Four or five episodes of fever induced by the blanket method, with temperatures of 104° to 105° F. (40° to 40.6° C.) were given during the treatment period

In the majority of symptomatic patients the clinical response was satisfactory, except, as was to be expected, in tabes dorsalis. Four patients with moderate or mild degrees of primary optic atrophy improved after treatment, though other severe cases were unaffected. The cell count, protein content, and colloidal gold reaction of the spinal fluid tended to revert to normal within one year, but the Wassermann reaction in both blood and spinal fluid usually remained positive. The authors agree that their results cannot be accurately compared with those of penicillin alone in the treatment of neurosyphilis.

G. L. M. McElligott

**754. Observations on Treatment of Cardiovascular System Syphilis with Aqueous Penicillin G**

S. A. M. JOHNSON and H. H. SHAPIRO. *Archives of Dermatology and Syphilology* [Arch. Derm. Syph., Chicago] 63, 426-432, April, 1951. 25 refs.

The authors treated 17 patients suffering from established cardiovascular syphilis with 4,008,000 units of aqueous benzyl penicillin. A gradually increasing dosage scheme was employed, beginning with eight 3-hourly injections of 1,000 units on the first day of treatment and rising to 40,000 on the eighth and subsequent days. Of the 17 patients, 5 died after 2, 270, 350, 527, and 854 days respectively. No Herxheimer reactions were encountered, but orthodiagnostic study revealed a subsequent worsening of cardiac damage in 7 patients, improvement in 3 patients, no change in 5, and equivocal results in 2 patients. The authors found orthodiagnostic control to be more sensitive than that of radiography or electrocardiography. Adjuvant treatment with heavy metals was not given.

[It is regrettable that no account is given of the necropsy findings, if any, in the patients who died.]

G. L. M. McElligott

**755. Aureomycin and Its Effect in Early Syphilis. Progress Report**

J. RODRIGUEZ, F. PLOTKE, S. WEINSTEIN, and W. W. HARRIS. *Archives of Dermatology and Syphilology* [Arch. Derm. Syph., Chicago] 63, 433-439, April, 1951. 4 figs., 1 ref.

This is a study of 67 patients with dark-field-positive early syphilis who were treated with 70 g. of aureomycin by mouth in 11 days. At the end of 6 to 7 months all the 3 primary sero-negative patients were clinically and serologically normal, as were also the 2 primary sero-positive ones. Of the 62 secondary cases, 37 became sero-negative, 13 had a weakly positive reaction of 3 Kahn units or less, 10 one of 4 Kahn units or more. One patient was thought to have been reinfected and another was classified as a muco-cutaneous relapse. The incidence of transient toxic effects of treatment was high, there being 50 cases of vomiting and 62 of nausea. High and sustained blood aureomycin concentrations were easily maintained by the oral route, and in one-half of the patients aureomycin was detected in the spinal fluid during treatment. The shortest time interval before a lesion became dark-field-negative was 17 hours and the longest 65 hours, the average time for a group of 25 patients being 39 hours.

[These preliminary results suggest that oral aureomycin may be reasonably effective in the treatment of early syphilis, but continued studies are necessary to determine its place, if any, in the therapeutic field.]

G. L. M. McElligott

**756. Mazzini Cardiolipin Microflocculation Test for Syphilis**

L. Y. MAZZINI. *Journal of Immunology* [J. Immunol.] 66, 261-275, Feb., 1951. 9 refs.

In this test the disadvantage of the slow "ripening" of the Mazzini lipoidal antigen emulsion has been overcome by using a variant which allows the emulsion to reach optimal sensitivity immediately after its preparation. This renders the test usable in emergencies and adaptable to a particular serological routine. An improved technique of preparing the emulsion and performing the test is detailed, whereby the cardiolipin-lecithin antigen becomes more efficient in both sensitivity and specificity.

The tendency of the antigen to produce a disproportionate number of zonal reactions with strongly positive sera has been overcome by decreasing the quantity of serum, adding saline after the primary rotation, and recentrifuging at a slower speed for an additional 4 minutes. Both specificity and sensitivity are increased, but false positive reactions continue to occur in many diseases other than syphilis. The test is applicable to spinal fluids, requires a very small amount of serum, and seems to be as sensitive and reliable as the complement-fixation test.

T. Anwyl-Davies

**757. The Effects of Sex, Castration, and Testosterone upon the Susceptibility of Rabbits to Experimental Syphilis**

H. J. MAGNUSON, B. J. ROSENAU, and B. G. GREENBERG. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [Amer. J. Syph.] 35, 146-163, March, 1951.

The authors took 46 adult male and 38 female rabbits; 22 of the former were normal and 24 castrated; 27 of the latter were normal and 11 spayed; each group was divided into three, one receiving no testosterone, one receiving 0.3 mg. per kg. body weight daily to a total of 13.2 mg. per kg., and the third 1 mg. per kg. daily to a total of 83 mg. per kg. Emulsions of *Treponema pallidum* ranging from 10 to  $10^6$  organisms were inoculated into 6 sites over the backs of the animals.

Results showed that the incubation period is shorter in males than in females, but the latter develop more lesions with the same inocula; castration in both sexes prolongs the incubation period and increases the resistance to infection; the shorter incubation period in the male is presumably due to more rapid division of the treponemata or to increase in the local reaction. Testosterone in increasing doses shortens the incubation period and increases the susceptibility in the male; in the castrated female large doses prolong the incubation period and increase resistance to infection. These paradoxical results suggest that testosterone interacts with sex factors, probably hormonal in nature.

T. E. Osmond

## Genito-urinary Disorders

### 758. Artificial Kidney: Preliminary Report

O. S. LOWSLEY and T. J. KIRWIN. *Journal of Urology* [J. Urol.] 65, 163-176, Feb., 1951. 4 figs., 21 refs.

A compact and efficient artificial kidney is described in which the dialysing membrane consists of sheets of cellulose instead of the usual cellulose tubing. The volume of blood in the machine at any one time is small (approximately 300 ml.), and no difficulties due to pyrogenic reactions were encountered during its use.

G. M. Bull

### 759. Chronic Glomerulonephritis with Severe Renal Tubular Calcification

D. ROSENBAUM, W. COGGESHALL, and R. T. LEVIN. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] 221, 319-324, March, 1951. 5 figs., 1 ref.

The authors describe what they believe to be the second recorded case of calcification of the renal tubules in chronic glomerulonephritis. The patient was 30 years of age, male, and had had attacks of acute nephritis in 1940 and 1942: on admission in 1949 he complained of central abdominal pain. Calcification of the kidneys could be seen on x-ray examination of the abdomen, especially in the renal cortex. The patient suffered severely from acidosis and died during a subsequent admission to hospital in the same year. The serum and urinary calcium levels had been normal, and the authors suggest that the condition was due to previous lower nephron nephrosis. Photomicrographs illustrate the condition of the kidney.

G. S. Crockett

### 760. The Pathogenesis, Diagnosis, and Anticholinesterase Treatment of Enuresis. (К патогенезу, диагностике и антихолинэстеразной терапии ночного энуреза)

R. K. IRKHO. Невропатология и Психиатрия [Neuropat. Psichiatr.] 20, No. 1, 84-88, 1951. 1 ref.

A series of 4 courses of treatment was given to 57 patients with nocturnal enuresis. The first course consisted of daily injections of distilled water given into the patient's arm without the patient being aware of the nature of the injection. During the second course distilled water was given into the gluteal region. If enuresis persisted 2 further courses were given, of eserine or "proserine" into the arm and into the gluteal region. A positive result was obtained in 48 cases, out of which injections of distilled water accounted for 12. Of the latter, improvement followed the injections into the arm in 8 and into the buttock in 4 cases.

The author suggests that the origination of enuresis may take place at any or all of the following levels: spinal cord, diencephalon, and cortex. He further suggests that cases of enuresis can be divided into an organo-neurotic, organic, and a psychoneurotic group. The treatment outlined above allows the recognition of

the 3 types. Those responding to water given into the arm are psychoneurotic, those responding to water injected into the buttock, which corresponds to the head zone for the bladder, may be regarded as organo-neurotic, while those responding to cholinesterase inhibitors, the majority in this series, are regarded as organic cases.

L. Crome

### 761. Tissue Changes in the Nephrotic Syndrome: Demonstration of Potassium Depletion

C. L. FOX and L. B. SLOBODY. *Pediatrics* [Pediatrics] 7, 186-192, Feb., 1951. 20 refs.

Specimens of muscle, liver, and kidney tissue, obtained at necropsy from 6 children dying from the nephrotic syndrome, were analysed and the results compared with those from 3 control subjects. In muscle the average water content was increased from 79% in the controls to 83% in the nephrotic subjects, sodium content was increased from 15 to 49 mEq. per 100 g. of tissue solids, and potassium content was reduced from 44 to 28 mEq. per 100 g. The water and electrolyte content of liver was unaffected. Kidney showed an increase in water and sodium content (and also in that of potassium, which is excreted in excess in the urine). Similar changes in muscle have been found after trauma, excessive cold, experimental potassium deprivation, alkalosis, and prolonged deoxycortone therapy.

D. M. Pryce

### 762. Paralysis with Potassium Intoxication in Renal Insufficiency. Value of Electrocardiographic Studies

R. A. MCNAUGHTON and H. B. BURCHELL. *Journal of the American Medical Association* [J. Amer. med. Ass.] 145, 481-483, Feb. 17, 1951. 2 figs., 7 refs.

The case is reported of a woman of 49 with bilateral renal calculi and pyelonephritis, who was admitted in a severe uraemic state. She had a complete flaccid paralysis of all limbs, but could speak and was mentally clear. The paralysis had come on gradually over the previous week. An electrocardiogram taken on admission showed the intraventricular block characteristic of the late phase of potassium intoxication. Serum content of sodium was low, that of potassium high, compared with the normal values. She was treated with an intravenous infusion of 5% dextrose in normal saline. Within 2 hours she had regained the power of her limbs completely. The electrocardiogram was nearly normal after 5 hours, and completely normal in 18 hours from starting treatment.

Great muscular weakness or even paralysis may be associated with deficient serum potassium, as during the treatment of diabetic coma or after an overdose of deoxycortone acetate. The electrocardiogram provides a clear and easy method of distinguishing between hyper and hypokalaemia.

Marianna Clark

## Disorders of the Locomotor and Osseous Systems

763. Effects of Pituitary Adrenocorticotropic Hormone (ACTH) in Rheumatoid Arthritis  
H. M. MARGODIS and P. S. CAPLAN. *Journal of the American Association [J. Amer. med. Ass.]* 145, 382-389, Feb. 10, 1951. 3 figs., 12 refs.

Short-term administration of ACTH in rheumatoid arthritis is almost invariably followed by relapse when the hormone is withheld. The authors decided to study the effects of long-term administration of this substance and to investigate the safety of such long-term administration and the means by which the remission, once induced, might be maintained. As gold is known to induce remission in certain cases, they studied the possibility of combining hormone therapy with subsequent chrysotherapy to maintain the remission.

The group which they studied totalled 56 patients; 46 of these were treated for periods of 2 to 7 months, the remainder for shorter periods: 23 patients were treated with gold and ACTH; 33 with ACTH alone. Tables are given to show the duration of disease, varieties of associated organic disease, age distribution, and dosage of ACTH employed.

Of the 56 patients, 40 responded satisfactorily to treatment with ACTH, 12 showed some improvement, and 4 did not respond. Of these last, 1 had very severe arthritis with ankylosis of many joints and 3 had severe psychoneurotic symptoms. In the patients who responded satisfactorily the degree of response depended on the degree of structural change which was present before treatment started, but the response to a first course of injections was not necessarily reproduced by subsequent treatment. Similarly, long-continued therapy was not necessarily accompanied by continued satisfactory response, and some patients deteriorated during such treatment. However, 7 patients who had responded satisfactorily remained in absolute remission for periods varying from 30 to 229 days after injections of ACTH had been withheld. All these 7 patients had been treated with gold as well as ACTH. In discussing the combination of chrysotherapy and hormone therapy the authors point out that their figures suggest that this combination may possibly be of greater value than hormone injection alone and may prolong the effect of hormone therapy.

The laboratory investigations which were made revealed the fall in number of circulating eosinophils when ACTH was administered, but the degree of fall could not be correlated with the degree of improvement which occurred. In most patients there was a prompt rise in haemoglobin level and fall in the erythrocyte sedimentation rate. The sedimentation rate tended to rise again when the amount of hormone administered was decreased or administration stopped. Half the patients developed side-effects, which in most instances were trivial; but it is notable that hypertension,

hyperglycaemia with glycosuria, osteoporosis, mental depression, and cerebral confusion did develop in certain cases.

The authors conclude that ACTH has now a definite place in the therapeutic armamentarium. They suggest from their experience that it will prove most beneficial in the early case and that serious side-effects are infrequent. They stress their finding that long-continued administration is followed by a falling-off in the degree of response and by an increased tendency to the development of side-effects. Stresses and strains decrease the improvement obtained with ACTH and increase the liability to relapse. They feel that further investigation should be made into the value of combined chrysotherapy and hormone treatment, and finally conclude that measures such as physiotherapy have by no means lost their value now that these new, potent preparations have arrived.

W. Tegner

764. Response of the Serum Hyaluronidase Inhibitor and Mucoproteins to Adrenocorticotropic Hormone in Rheumatic States. Mucolytic Enzyme Systems.

F. H. ADAMS, V. C. KELLEY, P. F. DWAN, and D. GLICK. *Pediatrics [Pediatrics]* 7, 472-481, April, 1951. 7 figs., 25 refs.

Adrenocorticotrophin (ACTH) was given, in doses of 40 to 100 mg. daily for an average of about 4 weeks, to 13 patients with acute rheumatic fever and 2 with juvenile rheumatoid arthritis: the ages of the patients ranged from 4 to 17 years. Prompt relief of their acute symptoms was observed.

The levels of the serum non-specific hyaluronidase inhibitor and of the serum mucoprotein tyrosine were especially studied. It was found that the hyaluronidase-inhibitor level fell rapidly during the administration of ACTH, reaching normal usually in 10 to 15 days and often becoming subnormal subsequently. This followed the fall in the erythrocyte sedimentation rate and the subjective improvement in the patient's condition. The fall in the serum mucoprotein level was much slower, and normal values were usually not seen for 3 or 4 months. This is in contrast to the findings in patients who have not received ACTH, but are treated symptomatically: in these the serum level of mucoprotein and of hyaluronidase inhibitor fall at about the same rate. If ACTH was withdrawn or reduced in dose before the serum mucoprotein level fell substantially, there was a recurrence of the disease even if the sedimentation rate and hyaluronidase-inhibitor level had returned to normal.

One patient had diabetes mellitus in addition to rheumatic fever. ACTH therapy necessitated an increase in the dose of insulin from 40 to 80 units daily. The clinical response was good, and similar to that of other patients: after ACTH was discontinued, the insulin requirements gradually returned to their former level.

Mild acne and slight fluid retention, not amounting to pitting oedema, were the only side-effects noted.

B. E. W. Mace

**765. Therapeutic Suppression of Tissue Reactivity.**  
**I. Comparison of the Effects of Cortisone and Aminopterin**

R. GUBNER. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] 221, 169-175, Feb., 1951. 47 refs.

The author draws attention to the similarity between the therapeutic activity of cortisone and the folic acid antagonist which is termed aminopterin. The result of his researches seems to show that the locus of their biochemical effects is not the same. Both substances are none the less anti-anabolic and tend to inhibit tissue regeneration. He also reports evidence for believing that aminopterin exerts an additional inhibitory effect upon various specific tissue elements, since the lesions of psoriasis are much improved and experimental and clinical arthritis also respond favourably. This, he believes, reflects a suppression of both epithelial and mesenchymal activity.

The author considers that diseases of tissue reactivity should be grouped nosologically as such, since in such cases it is the tissue reactivity which itself constitutes the disease process, and therapy might be aimed at suppressing this. He discusses the question of compounds other than cortisone and aminopterin which may selectively affect mesenchyme.

W. S. C. Copeman

**766. Effect of 17-Hydroxy-11-dehydrocorticosterone and Adrenocorticotropic Hormone upon Plasma Gamma Globulin, Fibrinogen, and Erythrocyte Sedimentation Rate**

J. H. VAUGHAN, T. B. BAYLES, and C. B. FAVOUR. *Proceedings of the Society for Experimental Biology and Medicine* [Proc. Soc. exp. Biol., N.Y.] 76, 274-277, Feb., 1951. 4 figs., 13 refs.

The authors have examined 17-hydroxy-11-dehydrocorticosterone (cortisone) and adrenocorticotropic hormone (ACTH) for their mechanism of action in relation to three blood elements. The observations were made on 12 hospital patients with severe, active rheumatoid arthritis and 3 with actively progressing, generalized scleroderma. Blood samples were obtained before, during, and after one or more courses of 100 to 200 mg. of cortisone acetate (aqueous suspension) daily or 80 to 100 mg. ACTH daily. Both compounds were given intramuscularly in divided doses at 6-hour intervals.

It was found that during hormone treatment the average fall in plasma  $\gamma$ -globulin level was from 105 to 67 flocculation units, in that of fibrinogen from 8.3 to 4.9 mg. per ml. and in erythrocyte sedimentation rate from 1.16 to 0.59 mm. per second. The inter-relationships of the estimations in individual cases are discussed. The authors conclude that the sedimentation rate cannot be used as an index of the effectiveness of hormone therapy on the active disease process.

Malcolm Woodbine

**767. Therapeutic Effect of an Allergic Reaction to Food on Rheumatoid Arthritis**

L. G. POLYMEAKOS. *Lancet* [Lancet] 1, 831-832, April 14, 1951. 5 refs.

**768. The Permeability of the Synovial Membrane. (La perméabilité synoviale)**

F. COSTE and M. BOUREL. *Rendiconti Istituto Superiore di Sanità* [R.C. Ist. sup. San.] 14, 32-82, 1951. 15 figs., bibliography.

**769. Some Observations on 100 Cases of Ankylosing Spondylitis**

L. J. A. PARR, P. WHITE, and E. SHIPTON. *Medical Journal of Australia* [Med. J. Aust.] 1, 544-549, April 14, 1951. 12 refs.

The authors studied 100 cases of ankylosing spondylitis from the eastern States of Australia. The ratio of males to females was 5 : 4—lower than those from English and American sources quoted. The average age at onset was 26 years. The disease was, on the average, milder in women than in men. Initial peripheral involvement was found in 6% of cases.

Associated factors such as the body build, climate, pre-existing tuberculous and gonococcal infections, and military service did not seem to be aetiologically important. Significant family history was elicited in 11% of cases.

Unlike rheumatoid arthritis, the ankylosing spondylitis manifested itself for the first time during pregnancy in 5 cases, and in a number of cases was aggravated by it. Iritis was recorded in 4% of cases. The erythrocyte sedimentation rate (E.S.R.) was raised in only 45% of cases; on the other hand, a number of symptom-free cases manifested a "much raised" E.S.R. for several years. [These findings contrast with those of Simpson and Stevenson (Brit. med. J., 1949, 1, 214), who found a definite correlation between the rise in E.S.R. and the severity of the disease.] Changes in plasma proteins did not differ from those recorded by previous observers and were similar to those found in rheumatoid arthritis.

The importance is stressed of an early clinical diagnosis and of the immediate institution of x-ray treatment before the appearance of unequivocal radiological signs, which may only appear some years (up to 7 in the present series) after the onset of symptoms. Morning stiffness, which disappears with exercise, in a young subject should at once arouse suspicions. Good response to x-ray therapy confirms the diagnosis in doubtful cases. The correct diagnosis had been made in less than half the recorded cases before examination by the authors, who therefore advocate a routine x-ray examination of sacro-iliac joints in all young adults complaining of vague rheumatic pains anywhere in the body for a year or more. X-ray therapy was found valuable in all stages of the disease; in only 4% of the cases was there no improvement at all. Early treatment is urged, however, to prevent disability.

A. Swan

## Neurology

### 770. An Experimental Study of the Effects of Ultrasonic Energy on the Lower Part of the Spinal Cord and Peripheral Nerves

T. P. ANDERSON, K. G. WAKIM, J. F. HERRICK, W. A. BENNETT, and F. H. KRUSEN. *Archives of Physical Medicine [Arch. Phys. Med.]* 32, 71-83, Feb., 1951. 5 figs., 15 refs.

The effects of ultrasonic energy on the lower part of the spinal cord and on peripheral nerves were investigated in albino rats and dogs. The effects observed were limited to changes in function as evidenced by clinical observation of paralysis and by changes in the nerve action potentials. Temperature variations in the tissues were also recorded and histopathological changes in nerve tissue were studied. Generally only maximal doses of ultrasonic energy were used in this study. Ultrasonic energy applied in these maximal doses over the lower vertebrae of both dogs and rats resulted in paralysis of the hind legs and tail. Total energy of 3.0 to 5.8 watts per sq. cm. applied to the mid-thigh over the sciatic nerve resulted in complete blocking of, or at least 50% decrease in, the action potential of the intact nerve in 60% of the dogs studied. Recovery of the nerve was usually complete when the action potential had been only partially decreased, but recovery was generally incomplete when the action potential had been completely blocked. The action potential of the sciatic nerve was decreased by direct heating to a similar extent to that produced by ultrasonic energy. With the same doses applied externally, ultrasonic energy had much greater destructive effects on the spinal cord than on the sciatic nerve.

Histological studies of the damage caused to the spinal cord and cauda equina were those of necrosis. In some sections dissolution and interruption in continuity of nearly all the tissue structures, including axis cylinders, myelin, and nerve-cell bodies, were demonstrated. However, little damage was seen in blood vessels and mesenchymal supporting structures. Destruction and degeneration of white matter had also occurred. There were nodular enlargements and fragmentation of axis cylinders. The changes found in the fibres of the cauda equina and spinal nerve roots were remarkably different in appearance from those occurring in the white matter. The material in the myelin appeared to be clumped in small, dense bands across the fibres, leaving clear, empty spaces between them.

In conclusion, the author gives two reasons for believing that the effects of ultrasonic energy on nerve tissue are other than those caused by the production of heat alone: (1) the occurrence of marked destruction of the cord when temperatures recorded in the spinal canal were as low as 42° to 43° C. after application of ultrasonic energy; and (2) sciatic nerves, of which the action potential was completely blocked by application

of ultrasonic energy, showed much less histological evidence of the unusual, regular pattern of degeneration of myelin which is an effect of heat than sciatic nerves in which the action potential had been similarly completely blocked by direct heating.

M. H. L. Desmarais,

### 771. A Method of Measuring Reflex Times Applied in Sciatica and Other Conditions due to Nerve-root Compression

D. S. MALCOLM. *Journal of Neurology, Neurosurgery and Psychiatry [J. Neurol. Psychiat.]* 14, 15-24, Feb., 1951. 8 figs., 11 refs.

The author has devised a technique for measuring the reflex time of the ankle-jerk and the knee-jerk and finds that this time is, constant in normal adults. When examining patients with compression of one nerve root by a protruded intervertebral disk, he found that with unilateral lesions there was a delay of 1 to 4 milliseconds in 5 out of 7 cases as compared with the normal side, while in the remaining 2 cases there was no difference between the two sides. To find out at what level this delay occurred he measured, at operation, the conduction time in the motor root past the compressed segment of the nerve and compared this with the conduction time in the corresponding root on the opposite side, and in 5 out of 7 cases there was a delay of 1 to 6.5 milliseconds; in the remaining 2 cases, where there was bilateral compression, no difference could be detected between the two sides. He concludes that the increased reflex time is due to delayed conduction through the compressed segment of the nerve. Clinical assessment of a diminished tendon reflex does not always run *pari passu* with a delay in conduction time.

J. W. Aldren Turner

### 772. The Pendulum and Pendulum-like Knee Jerks in Hemiplegia. (Маятниковые и маятниковообразные рефлексы у гемиплегиков)

N. K. BOGOLEPOV. *Невропатология и Психиатрия [Nevropat. Psichiat.]* 20, No. 1, 54-56, 1951.

Pendulum knee-jerks in hemiplegia are distinct from pendulum-like jerks. The author bases this conclusion on the study of 69 cases of the former and 32 cases of the latter. The pendulum reflex appears during the early stages of central paralysis and is associated with hypotonia, marked sensory disturbance, or some cerebellar involvement. The leg moves 6 to 8 times, and the movements are relatively slow and diminish gradually in amplitude. The pendulum-like jerks appear at a later stage together with spasticity and clonus. The movements are repeated 20 to 60 times and have a frequency of 1 to 3 per second and an amplitude of 40 to 45 degrees. They are associated with a combination of a pyramidal-tract lesion with a disturbance of deep sensation.

L. Crome

## 773. The Pendulum Knee-jerk. (О маятниковом коленном рефлексе)

L. I. SPIVAK. Невропатология и Психиатрия [Neuropat. Psichiat.] 20, No. 1, 56-57, 1951.

No good purpose is served by the grouping of pendulum knee-jerks into such categories as rhythmical, hypertonic, and cerebellar. Pendulum knee-jerks may be found in the absence of permanent organic lesions in cases of functional nervous disease and in depressive psychoses.

L. Crome

## ELECTROENCEPHALOGRAPHY

## 774. EEG and Cortical Electrograms in Patients with Temporal Lobe Seizures

H. JASPER, B. PERTUSSET, and H. FLANIGIN. *Archives of Neurology and Psychiatry* [Arch. Neurol. Psychiat., Chicago] 65, 272-290, March, 1951. 10 figs., 17 refs.

The authors have carried out electroencephalographic (EEG) and electrocorticographic studies on 91 patients operated upon for temporal-lobe seizures during the last 10 years at McGill University and the Montreal Neurological Institute. Electrographic and pathological findings are compared and are correlated with the results of surgical excision in 56 patients who were observed for from 1 to 10 years after operation. The results of the clinical follow-up have already been recorded by Penfield and Flanigin (*Arch. Neurol. Psychiat., Chicago*, 1950, 64, 491).

Pre-operative EEG studies indicated the presence of a primary cortical epileptogenic focus in one temporal lobe with varying degrees of transmission or activation of the opposite side in 71 cases (78%); in 53 the unilateral nature of the discharge was evident with standard scalp leads, but in the 18 others basal electrodes were required. In the remaining 20 patients (22%) the localized epileptic discharge shifted from one temporal lobe to the other or was bilaterally synchronous. In many patients [the exact number is not stated] the EEG was recorded during spontaneous or leptazol-induced seizures. The clinical onset of the attack was usually accompanied by general "suppression" in the EEG lasting some 5 to 10 seconds and followed by the appearance of typical rhythmic waves at 4 to 6 per second.

Definite abnormalities were noted in electrocorticograms taken from the exposed temporal lobe and adjacent areas in all 91 patients; these consisted of rapid sporadic spikes (10 to 60 milliseconds' duration), slow spikes (70 to 150 milliseconds' duration), high-voltage rhythmic discharges (2 to 6 per second), and delta waves. The incidence of these abnormalities is tabulated. Local electrical stimulation was of assistance in many cases [again the number is not stated]; frequently the patient's aura or entire habitual attack was reproduced. In one patient stimulation of the uncinate gyrus reproduced a typical clinical seizure and gave in the electrocorticogram an initial period of low-voltage, rapid, local discharge (too small to be recorded by scalp electrodes), associated with suppression of electrical activity from the remainder

of the temporal region; the patient experienced his olfactory aura and became unresponsive; 16 seconds after the end of stimulation high-voltage, 4-per-second discharges were recorded from all electrodes on the temporal lobe, and the automatic behaviour characteristic of the patient's attacks developed; this continued for 90 seconds after the low-voltage, irregular, slow waves of post-ictal exhaustion had appeared. It is suggested that this may be the usual sequence in cases of epileptic automatism of temporal origin. Comparison of electrographic and pathological findings indicated a general pattern of anatomical localization of lesions in patients with unilateral and bilateral pre-operative EEG abnormalities.

The results of surgical excision were much better in patients with unilateral abnormal discharges in the EEG; prognosis was poor following unilateral excision where bilateral abnormal discharges were noted. Results were also better the greater the amount of abnormal tissue (as determined by the electrocorticogram) that was removed.

The authors remark that less than half the patients had attacks which could legitimately be called "psychomotor", and they suggest substitution of the terms "behaviour automatism" or "temporal automatism" for attacks resulting from focal disturbance in the temporal lobe. [This is a very important paper.]

John N. Walton

## 775. Electroencephalogram in Subacute Progressive Encephalitis

W. COBB and D. HILL. *Brain* [Brain] 73, 392-404, 1950. 8 figs., 10 refs.

The authors have studied the electroencephalographic (EEG) findings in 5 cases of confirmed subacute encephalitis. The records showed similar characteristics with a degree of specificity which is diagnostic of this group of conditions. Progressive changes were noted in the EEG, consisting of the disappearance of the normal rhythm and the development of a generalized repetitive complex of high-voltage slow waves with paroxysmal occurrence and a tendency to periodicity as the disease progressed. This complex slow activity, having become periodic, was repeated at intervals of from 4 to 20 seconds, and each complex was followed by a few seconds of relative absence of activity from the record. During the complex electrical disturbance, involuntary movements and altered tone of the patient's musculature appeared and were continued during the period of electrical inactivity. At each examination the waves in the repetitive complex retained a striking constancy of form, but there was great variability from time to time and from subject to subject; however, the periodicity of the phenomena was common to all occasions and to all patients. As the disease progressed to a fatal termination (in 4 cases) the amplitude of all activity, normal and abnormal, appeared to decline.

The authors remark that the changes they describe are very similar to those occurring during the unconscious state following a generalized epileptic seizure. They suggest that possibly a common focal brain-area exists

which is responsible for synchronization of the periodic cortical phenomena, but no definite support was given to this hypothesis by pathological studies. The findings are discussed with reference to recent experimental work on animals.

[Readers interested in the problem of subacute encephalitis and in clinical electroencephalography are advised to read this important paper.]

John N. Walton

**776. Studies in Neurosurgical Electro-encephalography.**

**I. Standard Electrode Placement**

B. D. WYKE. *Journal of Neurosurgery [J. Neurosurg.]* 8, 289-294, May, 1951. 7 figs., 9 refs.

**777. The Development of Central Nervous Rhythms in the Electroencephalogram in Children.** (Über die Entwicklung zentralnervöser Rhythmen im Elektrencephalogramm des Kindes)

E. SCHÜTZ, H. W. MÜLLER, and H. SCHÖNENBERG. *Zeitschrift für die Gesamte Experimentelle Medizin [Z. ges. exp. Med.]* 117, 157-170, 1951. 4 figs., 24 refs.

To determine the character of the electroencephalogram (EEG) in relation to age groups a large number of children and infants were examined and the material so obtained analysed in respect of the electrical behaviour of the hemispheres. During the first year of life the EEG was dominated by trains of slow, arrhythmic waves of frequency 3 to 5 per second and of amplitude dependent on the state of consciousness (50  $\mu$ v. when awake and 100 to 120  $\mu$ v. in sleep or with eyes closed). Short rhythms of variable frequency and location appeared in between. During the second month of life a new type of rhythm was regularly observed, its frequency being about 12 to 15 per second and its location constantly over the central region. An essential change took place in the fourth month with the appearance of the central alpha-rhythm. It was still lacking in group formation and its frequency still slower than normal. Towards the end of the fourth month this rhythm could be observed over the occipital region as well. The alpha-rhythms were still interpolated with the slow arrhythmic waves. At the end of the first year the alpha-rhythm activity over the occipital region was almost equal to that over the central area. Between the first and fifth year the slow arrhythmic waves gradually decreased and were replaced by more and more normal alpha-rhythms. In the group aged 5 to 10 no fundamental difference from the EEG of an adult could be detected.

Comparison of the unipolar EEG in 262 infants showed that both hemispheres responded in similar manner. In the second year the first signs of an occasional difference between right and left became evident. Of 82 cases in the 1-to-10 age group, 39 were of fair symmetry, and in 33 the left and in 10 the right hemisphere was electrically the more active. Left-sided dominance was twice as frequent in girls as in boys, right dominance 2-4 times more frequent in boys, and full symmetry was equally frequent in the two sexes. F. F. Kino

**CENTRAL NERVOUS SYSTEM**

**778. The Use of Proserine in Organic Diseases of the Nervous System.** (Опыт лечения прозерином органических заболеваний нервной системы)

E. F. KULKOVA-DAVIDENKOVA and B. S. VILENSKY. *Невропатология и Психиатрия [Nevropat. Psichiat.]* 20, No. 1, 64-67, 1951. 1 ref.

"Proserine" [an anticholinesterase drug] was used in treating 201 cases of organic nervous disease. It was useful in many cases, although the improvement was often only temporary. It had no effect in striatal disease, and was less effective than neostigmine in myasthenia gravis. Its administration in disseminated sclerosis was often followed by some improvement, and it was also found useful in such conditions as myotonia atrophica, amyotrophic lateral sclerosis, residual forms of tick-borne encephalitis and of poliomyelitis, and in cerebellar disease.

L. Crome

**779. Proserine in the Treatment of Chronic Diseases of the Nervous System.** (Прозерин в клинике хронических заболеваний нервной системы)

P. M. TCHERNOGORIK, B. Z. VISHEVNIK, A. G. VOLKOVA, R. I. MOSKVINA, Y. V. KUGARO, and N. M. BAVELSKAYA. *Невропатология и Психиатрия [Nevropat. Psichiat.]* 20, No. 1, 68-70, 1951.

"Proserine" was used in the treatment of 194 cases of various chronic nervous disorders. It has had no ill-effects and could be safely given at any age. Its use is indicated in difficult, advanced, and long-lasting cases of organic nervous disease.

L. Crome

**780. The Use of "Proserine" in Association with Balneotherapy in the Treatment of the Sequelae of Spinal Injury.** (Опыт применения прозерина в комплексе сбальнеотерапией при последствиях травм позвоночника и спинного мозга)

M. L. BASHANSKYA. *Невропатология и Психиатрия [Nevropat. Psichiat.]* 20, No. 1, 70-73, 1951.

A series of 100 patients, mostly war invalids with gunshot wounds of the spine, were treated with "proserine" in combination with the usual methods of the spa regime, while a corresponding control series were given spa treatment alone. Proserine was found to be effective.

L. Crome

**781. The Visual Field Defects in Subacute Combined Degeneration of the Spinal Cord**

G. H. H. BENHAM. *Journal of Neurology, Neurosurgery and Psychiatry [J. Neurol. Psychiat.]* 14, 40-46, Feb., 1951. 4 figs., 29 refs.

Bilateral visual failure due to optic atrophy is a well-recognized but uncommon complication of pernicious anaemia. The author describes 5 cases which occurred in a group of 112 patients with subacute combined degeneration of the spinal cord. He paid particular attention to the visual-field changes in 3 of the cases and found that the essential defect was a scotoma of centro-caecal type, with a varying degree of contraction of the

peripheral field. The importance is emphasized of considering the possibility of subacute combined degeneration in patients with bilateral centrocaecal scotomata, and of carrying out appropriate investigations, such as a full blood count and gastric test meal, before making a diagnosis of tobacco amblyopia or chronic retrobulbar neuritis. The importance of this is that good response may be expected if liver treatment is started at an early stage of the disease.

J. W. Aldren Turner

### BRAIN AND CRANIAL NERVES

#### 782. Neuro-endocrine Syndromes and Ventricular and Cisternal Hydrocephalus. (Syndromes neuro-endocriniens et hydrocéphalies ventriculaires ou cisternales)

J. GUILLAUME, R. ROGE, and R. DJINDJIAN. *Semaine des Hôpitaux de Paris* [Sem. Hôp. Paris] 27, 876-884, March 18, 1951. 30 refs.

The authors conclude, on the basis of a study of more than 70 cases, that a mechanical factor may play a part in the production of endocrine syndromes of neurohypophysial origin. The cerebral lesion may be due to a chronic hydrocephalus acting on the diencephalo-hypophysial region by distension of the third ventricle, or to compression of that region by localized serous meningitis and collections of fluid in the cisterna chiasmatica. The authors have operated on a large number of these cases, performing either subthalamic ventriculostomy in the cases of hydrocephalus or anterior cisternostomy in the cases of basal serous meningitis. Most patients were either cured or much improved by these procedures.

The endocrine syndromes observed in patients operated upon consisted of: infantilism of various types, 30 cases; obesity, 18 cases; acromegaly, 7 cases; gigantism, 3 cases; pituitary basophilism, 3 cases. The neurological symptoms encountered were: headache (nearly always fronto-temporal) in 28 cases, accompanied by nausea and vomiting; convulsions, which occurred in 8 cases; and various ocular manifestations observed in 24 cases. These consisted of diminution of visual acuity in 10 cases, and alterations in the visual field in 11 cases. Superior bitemporal hemianopia was found in 7 cases. The fundus oculi showed changes in 15 cases, dilated veins in 2 cases, blurred edges of the disks in 5 cases, and early optic atrophy in 3 cases. Various psychological abnormalities were noted in 41 cases, and there was great improvement in some of these post-operatively.

[This paper is of great interest because endocrine symptoms are usually regarded as very rare accompaniments of chiasmal arachnoiditis, whereas the authors state that they may dominate the clinical picture.]

J. MacD. Holmes

#### 783. The Experimental Application of Ultrasonics to the Localization of Brain Tumors. Preliminary Report

L. A. FRENCH, J. J. WILD, and D. NEAL. *Journal of Neurosurgery* [J. Neurosurg.] 8, 198-203, March, 1951. 8 figs., 4 refs.

#### 784. Encephalitic Form of Metastatic Carcinoma

L. MADOW and B. J. ALPERS. *Archives of Neurology and Psychiatry* [Arch. Neurol. Psychiat., Chicago] 65, 161-173, Feb., 1951. 4 figs., 7 refs.

The authors describe 4 cases of diffuse spread of carcinomatous cells in the brain, meninges, and spinal cord. Clinically, the cases varied considerably, but the authors stress that the process should be suspected in middle-aged or older persons suffering from what appears to be a diffuse encephalitis. All the authors' patients had convulsions and signs of meningeal irritation, 3 had an organic mental syndrome, 3 had hemiparesis, and 2 presented with papilloedema without localizing signs. Pathologically, gross inspection of the brain revealed no significant abnormality. Microscopical study showed carcinomatous cells infiltrating the meninges of brain and cord. In the brain, diffuse infiltration of any area of the cerebrum, brain-stem, and cerebellum might occur, often with perivascular infiltration of the cells and extension from the meninges. In heavily infiltrated areas there was degeneration of the ganglion cells and increase in glial elements. The spinal cord might be involved in the same fashion. In 3 out of the 4 cases the primary carcinoma was in the lung—in the fourth case the primary site was not discovered. The incidence of the condition in a series of 106 cases of verified metastatic carcinoma of all types was 3.8%.

[The authors discuss their reasons for terming this condition "encephalitic", but these are not very convincing.]

J. B. Stanton

#### 785. Tuberculomas of the Brain. Report of One Hundred and Fifty-nine Cases

A. ASENJO, H. VALLADARES, and J. FIERRO. *Archives of Neurology and Psychiatry* [Arch. Neurol. Psychiat., Chicago] 65, 146-160, Feb., 1951. 12 figs., 17 refs.

The authors report, from the Institute of Neurosurgery and Neuropathology, Santiago, 159 cases of tuberculoma of the brain (97 verified), occurring in a series of 799 intracranial tumours (610 verified). Various aspects of the cases are discussed. Among general pathogenetic factors, the authors point out that the aboriginal and mestizo population of Chile is at present passing through a stage of tuberculization in which natural defences are absent and acquired defences diminished by their living conditions. In 55 cases contact with a tuberculous person was proved or strongly suspected. A definite extraneuronal tuberculous lesion was found in 86 cases, the site being pulmonary in 62. Of 49 cases of tuberculoma verified at necropsy, x-ray examination of the lungs showed no pulmonary lesions in 7. The authors stress that normal lung radiographs do not preclude a diagnosis of tuberculosis of the nervous system and that non-pulmonary primary lesions should not be ruled out. Of 97 verified cases of tuberculoma, the granuloma was solitary in 64 and multiple in 33. The solitary tumours were more frequent in the cerebral hemispheres than in the cerebellum. Calcification was rare. Symptoms were primarily those of raised intracranial pressure, more severe when the tumours were multiple, with or

without localizing features. Pneumoencephalography, ventriculography, carotid angiography, and electroencephalography were used as aids to diagnosis.

As regards treatment, surgery under streptomycin and para-aminosalicylic acid cover is advocated in suitable cases, after careful evaluation of the state of the primary lesion, the patient's general condition, and the possibility of total removal of the granuloma. If there is any possibility of the tumour being non-tuberculous, exploration must be attempted. The operation consists ideally of removing all identified growths with minimal excision of surrounding healthy tissue, or decompression and drainage of the ventricles through the lamina terminalis or by Torkildsen's operation. Of 10 patients treated surgically in this manner and receiving streptomycin, 2 died as compared with a mortality of 42 out of 82 in the same clinic before the era of streptomycin. Cases in which raised intracranial pressure was thought to be due to choroiditis or a recent tuberculous process and in which no localizing signs were present were successfully treated medically, but details are not given of these.

J. B. Stanton

#### 786. Therapy in Psychomotor Epilepsy

F. M. FORSTER. *Journal of the American Medical Association* [J. Amer. med. Ass.] 145, 211-215, Jan. 27, 1951. 13 refs.

A study was made of 87 cases of psychomotor epilepsy at the Jefferson Hospital, Washington, D.C. The series included 51 males and 36 females; psychomotor attacks occurred alone in 32 cases, with grand mal in 48, with both grand mal and petit mal in 5, and with Jacksonian epilepsy in 2. Before the advent of phenacetylurea ("phenurone") therapy in 1947, 38 of these patients were treated with phenytoin ("dilantin") (0.3 to 0.5 g. daily) and phenobarbitone (0.03 to 0.2 g. daily) together or separately. Of the 25 patients observed for an adequate period, 17 were greatly improved, 8 unaltered. The administration, in addition, of methoin ("mesantoin") or of tridione ("tridione") was ineffective. The frequency of attacks before treatment bore no relation to its efficacy, but brevity of history and the association of psychomotor attacks with grand mal improved the prognosis. Since 1947, out of a further 49 cases studied, the effects of treatment can be assessed in 27. All 27 patient were given drugs used in the earlier cases as a first measure, though not in such heroic dosage, and in 8 cases the attacks were controlled. In the other 19 cases phenacetylurea (phenurone) was employed in a dosage of 1.5 to 3.5 g. daily. In 13 cases the attacks were controlled, but in 4, owing to toxic effects, the drug was discontinued. Side-effects included depression (in 8 cases), restlessness and agitation, anorexia, vomiting, and haematemesis; one patient died of aplastic anaemia. A considerable number of patients in the series had electroencephalographic (EEG) temporal-lobe abnormalities evident only in sleep, and such patients were particularly liable to depression when taking phenacetylurea. In 5 cases which resisted all drug therapy and in which foci were demonstrated by the EEG

temporal lobotomy was performed; this gave complete relief in 2 cases and temporary improvement in 2; in one case an unsuspected glioblastoma was found.

Thus in approximately half the patients the attacks were controlled by phenytoin together with phenobarbitone; in about half the remainder phenacetylurea was effective, though toxic effects were severe; and in other cases surgery was of value. John N. Walton

#### 787. The Problem of Ophthalmoplegic Migraine.

(К вопросу об офтальмоплегической мигрени)

M. B. KHAIT. *Невроатология и Психиатрия* [Nevropat. Psichiat.] 20, No. 1, 60-63, 1951.

The literature relating to this subject is reviewed and 2 new cases are reported. The author concludes that while ophthalmoplegic migraine may be regarded as a variety of migraine, it is in some cases only a syndrome associated with manifold lesions of the brain. The pareses may be permanent. Localized angioneurotic oedema of the meninges at the base of the brain may lead to raised intracranial pressure. Like other forms of migraine, it is related to an instability of the endocrine-vegetative system, and particularly of the vegetative centres in the hypothalamus.

L. Crome

#### 788. Postherpetic Trigeminal Neuralgia

O. SUGAR and P. C. BUCY. *Archives of Neurology and Psychiatry* [Arch. Neurol. Psychiat., Chicago] 65, 131-145, Feb., 1951. 5 figs., bibliography.

The authors describe the unsatisfactory results from the many forms of treatment that have been tried in cases of post-herpetic facial neuralgia; they relate their experience of a patient on whom nearly all these procedures were performed within a few years.

The patient, a man aged 67, had herpes of the left cheek and the left side of the jaw which left him with a severe burning pain and occasional sharp exacerbations of severe, lancinating pain. He was treated successively by alcohol injection of the infra-orbital nerve, x-ray irradiation of the Gasserian ganglion, and fractional division of the sensory root of the left trigeminal nerve together with direct alcohol injection of the ganglion, followed 3 months later by complete sensory-root section. These procedures produced only temporary relief from pain, if any, as did subsequent cocaineization of the spheno-palatine ganglion and procaine block of the left stellate ganglion. At this point it was decided to attempt local extirpation of the contralateral sensory cortex. The area for the upper lip, tongue, and roof of the mouth was identified by stimulation under local analgesia and was removed. When the immediate post-operative disturbance had subsided, the sensory loss over the left side of the face resulting from the previous operations was found to be only slightly extended, and there was left-sided dysgeusia. The pain, moreover, returned on the fifth post-operative day and persisted. The ipsilateral (left) sensory face area was then removed, but subsequent microscopic examination showed the area removed to have been posterior to the post-central gyrus. There was no relief from pain following this operation, nor any sensory loss over the right face.

The patient continued his therapeutic Odyssey through 10 treatments of electric-shock therapy, and finally bilateral prefrontal lobotomy was performed. The pain apparently persisted, but did not distress him any longer. He died after an accidental fall.

The authors state that post-herpetic pain appears "almost entirely" in elderly persons with signs of arteriosclerosis; they suggest that hypoxia attendant on this allows perpetuation of widespread thalamo-corticothalamic circuits which are responsible for the persistent pain.

J. B. Stanton

**789. Retrobulbar Neuritis associated with Hyperthyroidism**

M. A. GOLDZIEHER, T. H. McGAVACK, C. A. PETERSON, J. W. GOLDZIEHER, and H. R. MILLER. *Archives of Neurology and Psychiatry* [Arch. Neurol. Psychiat., Chicago] **65**, 189-196, Feb., 1951. 4 figs., 13 refs.

A description is given of 2 cases of optic neuritis with changes in the nervous system in patients with thyroid dysfunction. In the first case a girl of 15 sought advice for loss of vision of the left eye, which had been coming on gradually for 4 years. The left fundus showed papilloedema and atrophy of the disk, and there was some atrophy and restriction of the visual field in the right eye. There was mild hyperreflexia in the left arm and leg. A few months later the patient developed symptoms of acute thyrotoxicosis with exophthalmos. She was treated medically without improvement in the visual acuity or exophthalmos.

The second patient, a woman of 35 years, developed thyrotoxicosis in 1943, with diffuse nodular enlargement of the thyroid and without ocular signs. She was treated medically until 1946, when she received a course of x-ray therapy. She remained free from symptoms for one year, after which she had symptoms of drowsiness and exophthalmos, and metabolic tests suggested that there was thyroid hypofunction at this time. There were no changes in the optic disks, but she had a small central scotoma with decreased visual acuity on the left. Exophthalmos rapidly became prominent in the next few months, and hyperthyroidism became manifest in metabolic tests. Slight blurring of the left disk became apparent and there was weakness of abduction and elevation of the left eye. Slight hypalgesia of the left side of the face and body was noted, with hyperreflexia of the left arm and leg. 18 months later subtotal thyroidectomy was performed, with rapid improvement in visual acuity in the left eye. Exophthalmos and ophthalmoplegia were unchanged, but the slight sensory changes disappeared and the deep reflexes were found to be symmetrically enhanced. In both cases the cerebrospinal fluid, radiographs of the skull, and the pneumoencephalogram were normal.

There is a review of some of the literature of neurological changes in thyroid disease. [In the first case the connexion of neurological changes with thyrotoxicosis appears to be rather distant, and it is perhaps surprising that the literature of exophthalmic ophthalmoplegia is not mentioned at all in connexion with the second case.]

J. B. Stanton

**MUSCULAR DISORDERS**

**790. Treatment of Myasthenia Gravis with Octamethyl Pyrophosphoramidate**

J. A. RIDER, S. SCHULMAN, R. B. RICHTER, H. C. MOELLER, and K. P. DUBOIS. *Journal of the American Medical Association* [J. Amer. med. Ass.] **145**, 967-972, March 31, 1951. 2 figs., 11 refs.

Of the various forms of alkyl phosphate compounds which have been tried in the treatment of myasthenia gravis during the past few years, tetraethyl pyrophosphate is the most effective, but suffers from the double handicap of toxic side-effects and rapid hydrolysis when exposed to moisture. Trials of a new anticholinesterase compound are described in this article—octamethyl pyrophosphoramidate, a drug which is very stable and is only slowly hydrolysed when exposed to moisture. This substance has been tried on 6 patients, 5 of whom were dissatisfied with, or responded poorly to, neostigmine. In addition to clinical impressions, efficacy of the drug was also gauged by estimation of the serum and the erythrocyte cholinesterase activity before and during treatment.

Octamethyl pyrophosphoramidate was administered orally as a 1% solution, the initial dosage being 7 mg. twice daily, rising by 1 mg. per dose every 1 to 3 days to a maximum of 18 mg., neostigmine being gradually withdrawn as this dose was built up. In 14 patients "successful" results were obtained in that these patients preferred the new drug to neostigmine; the action was evenly maintained when doses were given every 12 hours, and the resultant muscular strength in 3 cases was greater than that obtained with neostigmine. Mild side-effects included abdominal cramps, diarrhoea, and sweating, but these could easily be countered with atropine. Two cases were regarded as failures: of these 2 patients one died in a crisis while pyrophosphoramidate was being substituted for neostigmine; the other patient complained of epigastric pain and a lump in the throat and so the new drug was discontinued, although a satisfactory clinical improvement had been noted and the cholinesterase values had been depressed.

The drug's effect on the cholinesterase values is in itself interesting. The serum cholinesterase activity was depressed much more rapidly than that of the erythrocytes at first, although the latter reached a lower level finally. Maximum improvement in strength was not achieved until serum cholinesterase activity was 10 to 20% of the patient's normal and that of erythrocytes about 1%.

L. A. Liveredge

**791. Cholinesterase Activity of Blood and Muscle in Myasthenia Gravis**

A. WILSON, G. A. MAW, and H. GEOGHEGAN. *Quarterly Journal of Medicine* [Quart. J. Med.] **20**, 13-19, Jan., 1951. 2 figs., 15 refs.

The activity of pseudocholinesterase present in plasma and that of true cholinesterase present in erythrocytes, nervous tissue, and voluntary muscle did not differ in 19 patients with myasthenia gravis from that observed in normal subjects and in most animals. True cholin-

esterase activity varied over a wide range, but there was no significant difference as between its value in skeletal muscle removed from myasthenic patients during the operation of thymectomy and that in normal controls.

The mode of action of cholinesterase in blood and skeletal muscle of myasthenic patients did not differ from that of normal subjects, and the results of these experiments strengthened the conclusion that the fault in myasthenia gravis does not lie in an abnormally rapid destruction of acetylcholine.

Cholinesterase activity was determined manometrically by the method of Mendel, Mundell, and Rudney (*Biochem. J.*, 1943, 37, 473), the specific substrate benzoylcholine chloride (0.006 M) being used for the estimation of pseudo-cholinesterase and acetyl- $\beta$ -methylcholine chloride (0.03 M) for true cholinesterase.

W. H. McMenemey

#### 792. Cholinesterase Inhibition and Signs and Symptoms in Myasthenia Gravis

A. WILSON, G. A. MAW, and H. GEOGHEGAN. *Quarterly Journal of Medicine [Quart. J. Med.]* 20, 21-31, Jan., 1951. 4 figs., 14 refs.

Di-*iso*-propylfluorophosphonate (DFP), a potent and irreversible inhibitor of cholinesterase, was compared with neostigmine for its efficacy in the treatment of myasthenia gravis, the former being used in 10 cases for periods up to 2½ years. DFP was found to be unreliable, for it failed to relieve symptoms as effectively and consistently as neostigmine. Prolonged administration of DFP, which has the initial disadvantage of being administered as a solution in arachis oil, was necessary to allow of sufficient time for its diffusion from the blood to the tissues; even so its effect was erratic, the craniopharyngeal muscles, for instance, being more resistant to change than the peripheral muscles. Little evidence was found of any correlation between the relief of symptoms produced by DFP and its inhibition of the activity of the blood cholinesterases.

Intramuscular injection of neostigmine produced, along with the clinical response, only slight inhibition of the true cholinesterase of the erythrocytes. DFP, by contrast, inhibited the activity of the pseudocholinesterase of plasma to a greater extent than neostigmine, although unaccompanied by any immediate clinical effects.

When the small muscles of the hand were fatigued by electrical stimulation, injection of DFP into the artery of that arm, but not of the other, restored the action potentials to the pre-fatigue state, the effect of the drug being noticeable for as long as 4 days after the injection; the true cholinesterase activity of the venous blood from both arms was inhibited by about 20%. By contrast neostigmine restored the muscle action potentials in both hands, but the effect lasted for only 80 minutes, the true cholinesterase activity of the venous blood being inhibited by about 3%.

If the clinical effects of these drugs are due to their anti-cholinesterase activity, a possible explanation of the differences in clinical response to DFP and to neo-

stigmine is that the two drugs differ in their ability to reach and inhibit the cholinesterase of the motor end-plates, the difference in availability of the two compounds at the motor end-plates being possibly due to the fact that neostigmine combines reversibly with tissue cholinesterase, while DFP does so irreversibly. The effects of neostigmine, however, may be due to an action other than its anti-cholinesterase activity.

W. H. McMenemey

#### 793. Myopathy due to a Defect in Muscle Glycogen Breakdown

B. MCARDLE. *Clinical Science [Clin. Sci.]* 10, 13-33, Feb., 1951. 5 figs., 31 refs.

#### 794. Clinical and Physiological Studies in a Case of Myokymia

H. H. DE JONG, I. A. MATZNER, and A. A. UNGER. *Archives of Neurology and Psychiatry [Arch. Neurol. Psychiat., Chicago]* 65, 181-188, Feb., 1951. 9 figs., 9 refs.

The authors have carried out very extensive investigations on a single case of a condition which they designate as "myokymia". A white man aged 47 had complained of a gradually increasing cramping of his skeletal muscles after exertion over a period of 7 years, associated with excessive sweating, particularly of the feet, and coldness and cyanosis of the extremities. Examination revealed widespread rhythmic undulations of the muscles, which were most marked in the right gastrocnemius. There was a generalized increase in myotatic irritability, with some loss of power in the legs, but the reflexes and sensation were normal. Radiological and pathological investigations were also normal, and the response of all muscles to electrical stimulation was physiological. Electromyographic records revealed a regular rhythmic activity, at a discharge rate of 7 to 8 per second, in the gastrocnemius, right flexor carpi ulnaris, and right biceps muscles. According to the authors, this indicates the site of activity to be in the anterior horn cells of the spinal cord.

Spinal analgesia and local nerve blocks abolished the rhythmic discharge in the muscles affected. The administration of neostigmine and quinine caused no change in the rhythmic activity. Muscle biopsy showed normal motor-nerve end-plates.

The authors think that this condition is therefore unrelated to fasciculation, myoclonus, or tremor and should be regarded as a separate entity.

[The term myokymia is usually reserved for arrhythmic fascicular twitching observed as a transitory occurrence in normal persons, or for the similar twitching observed in toxic conditions where there is no evidence of specific abnormality of the central nervous system. The authors apparently wish to restrict the term to the entity described—namely, a state characterized by constant rhythmic undulations of muscle associated with cramp, but with absence of atrophy or histological change.]

Kenneth Tyler

# Psychiatry

## 795. The Psychosomatic Aspects of Cardiospasm

J. M. McMAHON, F. I. BRACELAND, and H. J. MOERSCH. *Annals of Internal Medicine [Ann. intern. Med.]* 34, 608-631, March, 1951. 46 refs.

A total of 25 patients (12 males and 13 females) with cardiospasm were subjected to psychiatric examination, each being interviewed at least three times. The mean age of the patients was 41 years; 4 were in the seventh decade, and there was one child of 12. The mean duration of symptoms was 9 years.

Of these patients 22 gave a history of neurotic traits, such as enuresis and phobias, in childhood. Neurotic traits in adult life, such as anxiety, depression, undue dependence on a parent, were noted in 23. Of the total, 18 were depressed at the time of examination; in the majority of these the depressive state was masked and was not apparent at the first interview. Some benefit was observed to follow in almost every case from talking over personal problems.

The onset of dysphagia followed psychic trauma in 24 cases. The 25th patient was a withdrawn individual with whom good rapport could not be established. The commonest emotional reaction at the time of onset was resentment. In 19 patients symptoms were more pronounced in the presence of emotional tension. A "secondary gain" from the illness was apparent in 3 patients.

Personality traits common to the group were: (1) perfectionistic, neat, orderly, meticulous; (2) submissive, lacking in aggression; (3) sensitive, easily offended; (4) shy, hard to approach, strong feelings of inadequacy; (5) reserved, tendency to hide feelings; (6) wish to be well thought of.

The authors conclude that cardiospasm is a disease of the frustrated and does not occur in happy and well-adjusted people.

Desmond O'Neill

## 796. The Metabolism of Glutamine and Glutamic Acid. (Glutamin- og glutaminsy-restofskifte)

P. ASTRUP and I. MUNKVAD. *Nordisk Medicin [Nord. Med.]* 45, 117-121, Jan. 24, 1951. Bibliography.

The metabolism of glutamine and glutamic acid is reviewed with special reference to the metabolism of nervous tissue. The normal concentrations in blood were found to be 6.19 to 9.98 mg. per 100 ml. of plasma for glutamine and 1.25 to 3.47 mg. per 100 ml. of plasma for glutamic acid. The concentration of glutamic acid is low and of glutamine is high in early cases of schizophrenia, in the active phases of chronic schizophrenia, in manic-depressive psychosis, and in epilepsy. Estimations made before, during, and after shock treatment showed that the glutamic acid level rose markedly, and the glutamine level fell less markedly, with the shock. The pre-shock levels were, however, regained after 20 minutes.

Margaret Agerholm

## 797. An Investigation into the Effects of Glutamic Acid on Human Intelligence

J. R. MILLIKEN and J. L. STANDEN. *Journal of Neurology, Neurosurgery and Psychiatry [J. Neurol. Psychiat.]* 14, 47-54, Feb., 1951. 20 refs.

The authors studied 23 adult mental defectives aged 21 to 29 years, 16 defective children with an I.Q. range of 41 to 66, aged from 10 to 14 years, and 56 normal boys between 10 and 15 years with an I.Q. range of 65 to 112 and 21 between the ages of 6 and 10 years with an I.Q. range of 67 to 112. These groups were each divided into experimental and control sections. The experimental section was given sodium glutamate, from 12 g. to 36 g. a day, while the controls received a mixture of yeast extract, sodium chloride, chloroform water, and water. The solutions were given for not less than 12 weeks in the normal groups and for 15 to 16 weeks in the defective groups. The control and experimental groups were then reversed and treatment recommended within a week. The subjects and the staff, including the psychologist, were unaware which subjects were receiving the sodium glutamate.

Vomiting or nausea occurred in more than 36 subjects after the sodium glutamate. Two boys, usually subject to violent outbursts of temper and difficult to manage, ceased to show temper while receiving the sodium glutamate, but reverted to their previous behaviour within 8 months after cessation of treatment. Increases in the I.Q. occurred over approximately 8 points in the experimental and control groups. The defectives and the junior normal boys were given 6 tests, the senior boys being given 7 other tests. In all these cases testing was performed before the start of the treatment, when the groups were reversed, and after the termination of treatment.

A group of 12 adult women mental defectives with an I.Q. ranging from 43 to 74 were treated with sodium glutamate for 4 months.

The cognitive test results gave no evidence of improvement in the tests. The results of ataxia and body-sway tests gave "the slenderest evidence" in favour of personality improvement. Improvement in Wechsler scores was unlikely to be due to improvement in alertness and speed. Difference in effects produced by glutamic acid and sodium glutamate cannot be due to different effects upon serum alkalinity.

[The title and summary are inaccurate. The authors set out to determine the value of glutamic acid but used sodium glutamate. Owing to the omission to push the dose until over-activity occurred in each case, the shorter period of treatment before re-testing, and the use of a different substance, this work neither confirms nor refutes that of Zimmerman *et al.*]

G. de M. Rudolf

**798. Treatment in the Mental Hospitals of the U.S.S.R. during 1949.** (Терапия в психиатрических больницах СССР в 1949 г.).

V. M. BANSHTCHIKOV and A. M. RAPOORT. Невропатология и Психиатрия [Nevropat. Psikhiat.] 20, No. 1, 32-47, 1951. 1 ref.

The methods of active treatment used in Soviet mental hospitals are reviewed on the basis of the annual returns for 1949. A critical statistical account is given of such methods as insulin shock, electric-convulsion therapy, prolonged sleep, artificially induced pyrexia, and prefrontal leucotomy. Prefrontal leucotomy has recently been banned (1951) in the Soviet Union, and it is therefore of interest that some of the larger hospitals had already begun to abandon it in 1949 on account of the unsatisfactory results obtained with this form of treatment.

L. Crome

**799. Effect of Prefrontal Lobotomy on Temperature Regulation in Schizophrenic Patients**

C. W. BUCK, H. B. CARSCALLEN, and G. E. HOBBS. Archives of Neurology and Psychiatry [Arch. Neurol. Psychiat., Chicago] 65, 197-205, Feb., 1951. 2 figs., 7 refs.

The authors, working at the University of Western Ontario Faculty of Medicine, have studied the temperature regulation of schizophrenics before and after prefrontal lobotomy. "The group comprised 40 schizophrenic patients, 38 males and 2 females: the median age was 32 years. The duration of illness at the time of operation varied from 1 to 8 years, with 80% of the patients falling into the 2- to 5-year range. Although all types of schizophrenia were represented in the group, the majority of cases (63%) were of the paranoid type."

The temperature regulation was studied (1) in the diurnal temperature-cycle and (2) in the response to heat and cold. In the first, 4-hourly rectal temperature measurements were made over a period of 4 days just before operation and over the same period 6 weeks after it. From the readings, group-means were calculated for (a) the mean temperature over the 4-day period, (b) the temperature range for each day, and (c) the day-night differential, that is, the difference between the means of the day and night temperatures. No change was observed post-operatively in the first 2 figures, but the third showed an increase to a value nearer to, but still differing significantly from, the value in normal people. (These last values had been obtained in a previous study.) It was therefore regarded as the best indication of the normality of the temperature cycle.

In the response to heat and cold, observations were made before, during, and after a 2-hour immersion in either a hot or a cold bath. The former showed no difference from the normal. In the cold bath the post-operative temperature curve showed a fall which began in the bath and continued after removal from it, and thus more closely resembled the normal than the pre-operative curve, which showed relatively greater stability in the presence of environmental temperature change.

In the second part of the paper the cases were subdivided into 2 groups (of 24 and 16 patients) according

to whether the duration of the illness was less than, or more than, 4 years respectively. The post-operative change was greater in those cases which differed most from the normal before operation, namely, in the group with relatively early psychoses.

J. P. Dewsbury

**800. Clinical and Psychological Investigation of Pre-frontal Lobotomy in Chronic Schizophrenia**

H. B. CARSCALLEN, C. W. BUCK, and G. E. HOBBS. Archives of Neurology and Psychiatry [Arch. Neurol. Psychiat., Chicago] 65, 206-220, Feb., 1951. 9 figs., 8 refs.

This study of 49 chronic schizophrenic patients in whom lobotomy had been performed deals with: (1) the changes in group trends before, and at intervals up to 6 months after, operation; (2) the value of certain factors in assessing the chances of improvement; and (3) the changes in intellect before, and at intervals up to 6 months after, operation.

(1) Group trends are studied under the headings of (a) behaviour, (b) affect, (c) hallucinations, and (d) delusions, and were assessed before, and 3 weeks, 3 months, and 6 months after, operation. Behaviour at the end of the period showed an improvement in that there were no longer any patients who were consistently disturbed and fewer who were intermittently disturbed; there was an increase in the number of abnormally seclusive patients. Affect, already dulled by the disease, remained consistently unchanged at all intervals after operation as compared with pre-operative assessments. Hallucinations were less readily demonstrated immediately after operation and there was a larger number in whom they could not be demonstrated at all. Later assessments, however, showed a trend back to the pre-operative state. Delusions showed a similar reduction immediately after operation, but similar increases at 3 and 6 months.

(2) The 4 factors examined in relation to improvement were: (a) previous response to electric-shock therapy; (b) response to previous insulin therapy (in neither was there any relation to improvement after operation); (c) age at time of operation (there was a tendency to poorer results in the younger patients); (d) duration of illness at the time of operation (there was a fall in the number of favourable results when the illness had lasted 5 years or longer). In neither (c) nor (d) were the results statistically significant.

(3) The verbal, performance, and full-scale intelligence quotients were assessed before, and at the above-mentioned intervals after, operation. Each showed a diminution at the 3-week interval, with a progressive improvement at the next two intervals to levels above the pre-operative one, the trend being most marked in the performance scale.

J. P. Dewsbury

**801. Experimental Physiological Studies with Lysergic Acid Diethylamide (LSD-25)**

G. R. FORRER and R. D. GOLDNER. Archives of Neurology and Psychiatry [Arch. Neurol. Psychiat., Chicago] 65, 581-588, May, 1951. 3 refs.

See also Section Radiology, Abstract 519.

## Infectious Diseases

### 802. Penicillin Treatment of Infectious Mononucleosis. Comparison of Effects in Ninety-nine Patients with and in Sixty-seven Patients without Penicillin Therapy

T. BENNIKE. *Archives of Internal Medicine [Arch. intern. Med.]* 87, 181-189, Feb., 1951. 2 figs., 35 refs.

During the period October, 1948, to July, 1949, 166 patients with infectious mononucleosis of the anginose type were admitted to the Epidemic Hospital, Copenhagen; 37% of them were under the age of 10 years. Penicillin was given in 99 cases in a dose of 120,000 to 300,000 units daily for the purpose of assessing the possible therapeutic value of this drug in glandular fever. The remaining cases were treated on conservative lines and served as a control group.

The course of the disease was found not to be influenced by penicillin on comparing the results in the two groups with special reference to the clinical response, duration of fever, length of stay in hospital, and incidence of excessive fatigue during convalescence. Pyogenic complications occurred rarely in both groups and were slightly less frequent among penicillin-treated patients.

G. B. Forbes

### 803. Dehydration Treatment of Rheumatic Fever

W. S. C. COPEMAN and L. G. C. E. PUGH. *Lancet [Lancet]* 2, 675-676, Dec. 2, 1950. 3 refs.

It has been suggested that salicylates owe their good effect in rheumatic fever to a reduction of the water content of the body cells. This hypothesis would be strengthened if similar results were obtained by dehydration alone.

Seven male patients with rheumatic fever were subjected to a course of treatment which included limitation of fluids, sodium sulphate by mouth, and intravenous hypertonic saline. Within 24 hours signs and symptoms were reduced, and side-effects were noted similar to those occurring during massive salicylate therapy.

David Nicholson

### 804. A Case of Sjögren's Syndrome Treated with Adrenocorticotrophic Hormone. [In English]

M. FRENKEL, G. HELLINGA, and J. GROEN. *Acta Endocrinologica (Copenhagen) [Acta endocrinol., Khb.]* 6, 161-182, 1951. 21 figs., 14 refs.

A case of Sjögren's syndrome is reported. The patient, a woman of 51, was given 50 mg. ACTH on the first day, then 30 to 40 mg. daily, the dosage being gradually reduced. Treatment was continued for 31 days. At the end of the first week of treatment the swelling of the parotid and lacrimal glands began to diminish, and in a fortnight had completely disappeared. After 3 weeks salivation returned, the lingual mucosa regenerated, and the tongue became completely normal in appearance. Lacrimal secretion also returned and the white filaments and erosions disappeared from the

cornea. Fever subsided and there was marked euphoria. There was no joint involvement in this case even before treatment, except for occasional pain and crepitus in the knees. Improvement was maintained in spite of reduction in the dosage, but the parotid swelling and dryness of the mouth returned one month after treatment was discontinued.

During treatment the eosinophil count fell, neutrophil count rose, blood uric acid : creatinine ratio and urinary 17-ketosteroid excretion rose, and the erythrocyte sedimentation rate fell. Detailed metabolic studies were carried out; there was retention of water and sodium, a fall in haemoglobin level, haematocrit reading, and serum protein level, slight hypochloraemia, and marked hypopotassaemia, the latter being accompanied by signs of over-action of the heart and the characteristic electrocardiographic changes.

Towards the end of treatment spasm of the central artery of the right retina developed, with loss of vision which had recovered only to the extent of light-perception at the time of the report. It was not clear whether or not this was the result of treatment with ACTH; the authors could trace no previous report of such a complication.

Robert de Mowbray

### 805. Trial of a Cinchoninic Acid Derivative in Some Collagen Diseases

J. B. RENNIE, J. A. MILNE, and J. SOMMERSVILLE. *British Medical Journal [Brit. med. J.]* 1, 383-388, Feb. 24, 1951. 6 figs., 7 refs.

This report from the Western Infirmary, Glasgow, describes the effect of 3-hydroxy-2-phenylcinchoninic acid (HPC) in 12 cases of collagen disease. The oral dosage varied from 20 to 40 mg. per kg. body weight for 1 to 3 weeks. Fever and painful joints were relieved in 4 cases of rheumatic fever, and joint swelling rapidly disappeared in 2 out of 3 cases. A rapid partial fall in the erythrocyte sedimentation rate coincided with treatment in 2 cases. Heart size, quality of sounds and murmurs, and subcutaneous nodules were uninfluenced. Two patients relapsed following withdrawal of HPC. In 1 out of 2 patients with polyarteritis nodosa HPC appeared to shorten the illness. The raised blood pressure fell to normal, fever, tachycardia, and alimentary symptoms disappeared, while fundal lesions regressed. Slight albuminuria and haematuria persisted. Striking clinical and histological improvement occurred in 3 patients with scleroderma, but 2 patients relapsed later.

Skin lesions in 3 cases of lupus erythematosus were thought to be less florid during HPC treatment, but this was not confirmed histologically. Toxic effects, which were infrequent, consisted of slight nausea, diarrhoea, and (rarely) vomiting.

I. Ansell

**806. Observations on Paragonimiasis at the Quezón Institute.** (Observaciones sobre la paragonomiasis en el Instituto Quézón)

M. CANIZARES and J. CELIS. *Revista Española de Tuberculosis* [Rev. esp. Tuberc.] 20, 39-46, Jan., 1951. 6 figs.

An account is given of 5 cases of paragonimiasis observed at the Quezón Institute in the Philippine Islands. The symptoms in all patients were very similar: a history of troublesome cough, pain in the chest, shoulder, and abdomen, and blood-tinged sputum which had been noted for periods varying between 9 months and 8 years. Eosinophilia ranging from 8 to 13% was present.

The first patient, a woman of 30, was given 40 ml. of stibophen (equivalent to 340 mg. of antimony) in 2 weeks, but the ova in the sputum did not seem to decrease. "Lipiodol", 10 ml., was then injected intrabronchially and the number of ova diminished markedly, but 3 days later on re-examination large numbers were again found. Though the symptoms are said to have improved, "the therapeutic result was far from satisfactory". The second patient, a woman of 22 years, was treated with stibophen to a total of 16 ml. (135 mg. of antimony); by reason of severe vomiting the full dose of 40 ml. could not be given. Again, although the patient was free of symptoms, the ova persisted in the sputum. The third patient, a man of 40 years, was given 3 intramuscular injections of 5 ml. of "prontosil soluble". For family reasons—he had a wife and 4 children—he had to leave hospital. During his stay he had one attack of haemoptysis. The fourth, a woman of 20 years, was treated with emetine hydrochloride "one-third grammie [sic] injections daily for 6 days, repeated after an interval of three days' rest in bed". The sputum, which previously contained ova in large numbers, was then free, as were the faeces, and repeated examination during the ensuing year also proved negative. The fifth patient, a man of 22 years, was treated with *p*-aminosalicylic acid for tuberculosis, 400 g. in all during 8 months. He then had another haemoptysis and 5 examinations of the sputa failed to disclose either acid-fast bacilli or ova. The latter were, however, found by bronchial aspiration, but in small numbers. This patient decided that he would "prefer to be treated by a parasitologist of his own choice" and left hospital at his own request.

[Of all the forms of treatment tried, emetine hydrochloride was the only one to prove successful; it would seem to be worthy of further trial.]

H. Harold Scott

VIRUS INFECTIONS

**807. Cat-scratch Fever. A Disease Entity**

W. E. R. GREER and C. S. KEEFER. *New England Journal of Medicine* [New Engl. J. Med.] 244, 545-548, April 12, 1951. 2 figs., 19 refs.

"Cat-scratch fever", a term first used by Foshay, is suggestive of, but milder than, tularemia. A contact with cats is invariable. Although the disease is associated with general systemic disturbance, the brunt of the

infection is borne by the lymph nodes. The infecting agent is probably a virus, and an antigen which produces a specific skin reaction when injected intradermally can be prepared from the pus of the buboes. The authors describe a case in a male aged 36 who, a fortnight before admission, was licked on the left side of the neck and scratched on the right hand by his cat. Four days later he noticed a painless swelling on the left side of the neck which increased to the size of a hen's egg. A few days later he felt weak, tired, and chilly, and 2 days before admission he developed a pinkish macular rash over the extensor surfaces of the arms with gradual development of small vesicles. Foshay's "cat-fever" antigen gave a strongly positive reaction, whereas its injection into 6 controls was without effect. French workers are under the impression that aureomycin shortens the course of the disease. The authors discuss the various diseases that may be transmitted to man by the domestic cat.

D. Prieskel

**808. Coricidin in the Treatment of the Common Cold**

M. H. MANSON, R. L. WELLS, L. H. WHITNEY, and G. BABCOCK. *International Archives of Allergy and Applied Immunology* [Int. Arch. Allergy] 1, 265-274, 1951. 40 refs.

From September, 1949 to April, 1950, the authors treated 8,583 patients living on the eastern seaboard of New Jersey for the "common cold". Three medications were used, "coricidin" (an antihistaminic-analgesic-antipyretic preparation), an equivalent drug without the antihistamine drug, and a placebo. Relief of the symptoms was noticed more frequently with the antihistamine compound than with the others. [The results do not seem convincing. The majority of cases was seen by nurses only. The relief was assessed by the patients. It is not clear from the paper in what way "allergic colds" were excluded from the survey.]

K. Maunsell

**809. The Epidemiology of Jungle Yellow Fever in South America.** (Die Epidemiologie des Buschgelbfiebers in Südamerika)

R. LEVI-CASTILLO. *Zeitschrift für Tropenmedizin und Parasitologie* [Z. Tropenmed. Parasit.] 2, 315-322 and 453-455, Jan., 1951. 1 fig., bibliography.

Jungle yellow fever in South America is due to the pantropic virus and has been reported to be present in all South American countries except Uruguay, Chile, and the Argentine. The insect hosts include species of the genus *Haemagogus*, *H. spegazzini* being the most significant, though other mosquitoes, especially of the *Aedes* group, are of importance. Monkeys form a reservoir of infection, but as they either die or recover rapidly from the disease (with production of immune bodies) they do not, individually, carry the disease for more than a few days. Since the disease is propagated by mosquitoes, jungle clearings and rivers constitute natural barriers against its spread.

Man acquires the fever by chance, and his presence is not essential for the continuation of the disease. He may

suffer from a slight infection, or the attack may be severe and fatal: in man, as in monkeys, the peripheral blood is infective for only a few days. The population at risk includes lumbermen, planters, and hunters. Certain conditions must be fulfilled before an epidemic can occur, and both susceptible, non-immune individuals and large numbers of infected mosquitoes are required. Since these conditions are seldom present the disease seldom reaches epidemic proportions. In epidemics the insect host is *Aedes aegypti*.

[This article gives a brief account of jungle yellow fever: it contains no original work, but is followed by a comprehensive bibliography, no mention of which is made in the text.]

W. H. Horner Andrews

**810. Age Incidence and Seasonal Development of Neutralizing Antibodies to Lansing Poliomyelitis Virus**  
T. B. TURNER, D. H. HOLLANDER, S. BUCKLEY, U. P. KOKKO, and C. P. WINSOR. *American Journal of Hygiene* [Amer. J. Hyg.] 52, 323-347, Nov., 1950. 8 figs., 32 refs.

The authors have carried out an extremely comprehensive study of the epidemiology of poliomyelitis in Baltimore City. Among the questions investigated were: (1) the total incidence of infection; (2) the level of infection in different age groups; (3) the seasonal variations in infection; and (4) the proportion of infections associated with clinical manifestations.

Clinical and serological findings were obtained from 970 persons, the majority being children less than 15 years old, who were admitted to the Johns Hopkins Hospital, Baltimore, between the years 1941 and 1948. Physical examination was carried out on each patient, and serum samples taken at intervals. In the routine neutralization test equal volumes of serum were stood for one hour with 200 LD<sub>50</sub> of Lansing poliomyelitis virus; 8 mice were inoculated with each mixture and the results recorded as positive if more than half survived the 21-day period of test.

Neutralizing antibodies were present in 72% of sera from infants less than 3 months old. The number of positive sera decreased rapidly thereafter until a figure of approximately 10% was reached at the end of the first year. The proportion then increased to 50% at 4 years, 72% at 5 to 9 years, 84% at 10 to 14 years, and 90% at 15 years and over. There was no significant variation with sex, but negroes showed a higher infection rate than whites. In no case did the serum test revert from positive to negative during the 7-year period of the test, but the data do not indicate whether this is due to the persistence of antibody or to repeated "booster" infections. Approximately 20% of previously negative children become positive each year. Infection was largely confined to the summer months, reaching a peak during August and September as judged both by notification of cases and appearance of antibodies.

A mathematical model was developed to express infection rates. Families of curves were constructed taking into account the dynamic equilibrium existing between immune and non-immune sections of the population. On this basis theoretical attack rates and

age-distribution curves were calculated and found to agree within experimental error with those obtained from observational data. An estimate of mean annual attack rate at any age level can also be made from such curves.

J. F. McCrea

See also Section Hygiene and Public Health, Abstracts 440-41.

### RICKETTSIAL INFECTIONS

**811. Typhus at Belsen. II. Clinical Course of Epidemic Typhus in Persons who had Received Craigie Typhus Vaccine**

W. A. DAVIS. *Annals of Internal Medicine* [Ann. intern. Med.] 34, 448-465, Feb., 1951. 4 figs., 14 refs.

The author describes the clinical course of epidemic typhus in three groups of persons. The first group consisted of 14 British troops who had been vaccinated with Craigie typhus vaccine more than 24 days before the onset of their fever. The second group consisted of 15 Hungarian troops who had received only 1 or 2 doses of Craigie vaccine after exposure to typhus, and the third group consisted of 41 German troops who had no vaccine.

Craigie vaccine is a polyvalent vaccine containing the soluble antigens and killed bodies of both epidemic typhus rickettsiae (*Rickettsia prowazekii*) and murine typhus rickettsiae (*Rickettsia mooseri*). The author classifies his cases from "very mild" to "fatal" and gives detailed clinical descriptions of several of them.

No deaths occurred in persons who had been vaccinated, although there were deaths in the non-vaccinated group. This is not, however, statistically significant, owing to the small size of the groups and the low death rate. The duration of the fever in the British and Hungarian troops was much briefer than in the German and these figures are highly significant, the difference between the two groups being 10.3 times the standard error of difference. In fact, coupled with the clinical observations, the figures lead to the conclusion that 2 or more doses of Craigie vaccine (1 ml. each) given 24 or more days before the onset of louse-born typhus reduced the severity and shortened the course of the disease. Even given after exposure to typhus the vaccine was of some value in lessening the severity of the illness; the results add weight to the growing evidence that vaccination against typhus is of value even during an epidemic.

J. V. Armstrong

**812. The Symptomatology of Typhus Fevers. (Zur Symptomatologie des Fleckfiebers)**

H. R. FRANK. *Zeitschrift für Tropenmedizin und Parasitologie* [Z. Tropenmed. Parasit.] 2, 322-326, Jan., 1951. 11 refs.

Alopecia of the lateral surface of the leg was noticed during a routine neurological examination in a convalescent case of typhus. Further observations showed that out of 32 cases, this phenomenon was absent in 2 slight in 1, definite in 27, and very marked in 1. The

author can find no mention of this sign in the literature, but he points out that neurological dysfunctions are known to occur in typhus, and also that a falling out of hair may follow in the wake of nerve damage. He believes that the alopecia was due to toxic neuritis, especially of the lateral cutaneous nerve of the thigh, though the medial cutaneous and saphenous nerves were occasionally involved. The condition occurred bilaterally.

W. H. Horner Andrews

**813. Brill's Disease. II. Etiology**

E. S. MURRAY and J. C. SNYDER. *American Journal of Hygiene* [Amer. J. Hyg.] 53, 22-32, Jan., 1951. 1 fig., 24 refs.

The authors describe the isolation of 7 strains of typhus rickettsiae from 14 cases diagnosed clinically as of Brill's disease. They report in detail laboratory tests of these 7 strains in cotton rats, mice, guinea-pigs, and chick embryos, and discuss the aetiology of Brill's disease in the light of these animal experiments as correlated with results of serological tests. They used the following procedures for differentiating the 7 recently isolated strains: (1) cross-immunity tests in cotton rats; (2) virulence tests in newly-weaned white mice; (3) cross-immunity tests in newly-weaned white mice; (4) tests on sera of human patients; (5) tests on sera of experimentally infected guinea-pigs; (6) control tests. As controls they used the Breinl strain of *Rickettsia prowazekii* (epidemic typhus) and the Wilmington strain of *R. mooseri* (murine typhus).

The authors consider that the fact that the 7 new strains from Brill's disease induced solid immunity in cotton rats to several fatal doses of a known epidemic strain clearly established the organisms as typhus rickettsiae (murine or epidemic). They found that the virulence test in weanling white mice facilitated the differentiation of epidemic from murine typhus. Their results agreed with those of Mooser, who emphasized that without exception murine strains, inoculated intra-abdominally, multiplied profusely in the peritoneal cells of mice, whereas classic epidemic strains usually fail to do so. They found that the complement-fixation test, when performed with specially prepared rickettsial antigens, is a valid and accurate technique for separating both epidemic typhus and Brill's disease from murine typhus.

They concluded that their experiments strongly support the view that Brill's disease is a recrudescence or relapse of classic epidemic typhus. To prove this finally, however, it would appear to be necessary to isolate *R. prowazekii* from healthy individuals who are known to have had typhus in the past.

J. V. Armstrong

**814. Rickettsialpox Case due to Laboratory Infection**

M. H. SLEISINGER, E. S. MURRAY, and S. COHEN. *Public Health Reports* [Publ. Hlth Rep., Wash.] 66, 311-316, March 9, 1951. 1 fig., 5 refs.

See also Section Hygiene and Public Health, Abstracts 438-39.

**BACTERIAL INFECTIONS**

**815. Indeterminate Leprosy. A New Clinical Variety**  
G. H. FINDLAY. *British Journal of Dermatology* [Brit. J. Derm.] 63, 100-104, March, 1951. 1 fig., 6 refs.

It has been held for many years that there are two main types of leprosy, the tuberculoid (neural or maculop-anaesthetic) and the lepromatous (cutaneous, tuberous). During the last 10 years cases have been reported in which both types of the disease occur, and at the Havana Conference in 1948 particular attention was paid to these indeterminate cases. In this article such a case is reported in a Bantu woman aged 24, in whom both lepromatous and tuberculoid lesions were present before sulphetrone therapy was started. The tuberculoid lesions were virtually free from *Mycobacterium leprae*, while the lepromatous areas showed abundant bacilli.

H. R. Vickers

**816. First Cases of Primary Pneumonic Plague Successfully Treated with Streptomycin.** (Premiers cas de guérison de peste pulmonaire primitive par la streptomycine)

F. ESTRADE. *Presse Médicale* [Pr. Méd.] 59, 328, March 17, 1951. 3 figs., 5 refs.

The treatment of 2 cases of primary pneumonic plague with streptomycin is described. The dosage employed was, in the first case, 1.5 g. (given at night), then 4 g. daily for 5 days, followed by 2 days when 3.25 g. and 1 g. were given respectively. The second case was more severe, and 4.75, 6, 6, 4, 3, and 2 g. were given on 6 successive days. The results were highly satisfactory, and 20 hours after starting treatment the sputum was non-infective when placed on the shaved skin of a guinea-pig. Both patients recovered. Serial radiographs were taken of the lungs during the course of the disease and the author believes that radiological diagnosis is of special value for those exposed to the pulmonary infection.

W. H. Horner Andrews

**817. Neurological Complications of Undulant Fever. The Clinical Picture**

A. NELSON-JONES. *Lancet* [Lancet] 1, 495-498, March 3, 1951. 2 figs., 17 refs.

The author presents the picture of neurobrucellosis as it emerges from the foreign literature. The clinical picture is varied, but its special characteristics are meningotropism, liability to late onset months or years after the septicaemic state of undulant fever, and a tendency to produce a series of clinical recurrences in varying sites. It may be caused by *Brucella abortus*, *Br. melitensis*, or *Br. suis*. The neurological complications recorded are leptomeningitis, adhesive arachnoiditis, hypertrophic pachymeningitis, encephalitis, psychosis, inflammation of the ventricles, myelitis, radiculitis, neuritis, and neuralgia. Reports of 5 cases (one seen recently in London) are given. Drenching sweats, enlargement of spleen and liver, joint pains, orchitis, relative or absolute increase of lymphocytes or large mononuclears in a normal or low total leucocyte count and a history of raw-milk consumption are of importance.

for the differential diagnosis. The diagnosis may be strongly suspected if the agglutination titre to one of the *Brucella* groups is over 1 in 40 in the blood or cerebrospinal fluid and may be presumed if it is over 1 in 100. These tests may, however, be repeatedly negative and so may the blood culture. The brucellin intradermal test, complement-fixation test, and the opsonin cytophagic test are of value in the diagnosis.

The treatment consists of repeated lumbar puncture and passive and active immunization. The author advocates routine investigation for brucellosis in cases of neurological and mental illness in districts where raw milk is drunk.

*Margaretha Adams*

**818. Effect of Cortisone on Acute Streptococcal Infections and Post-streptococcal Complications**

E. O. HAHN, H. B. Houser, C. H. RAMMELKAMP, F. W. DENNY, and L. W. WANNAMAKER. *Journal of Clinical Investigation* [J. clin. Invest.] 30, 274-281, March, 1951. 4 figs., 32 refs.

This paper describes a controlled investigation undertaken at a U.S. Air Force base, in which 87 patients with streptococcal tonsillitis or pharyngitis were given injections of cortisone acetate (total dose 500 to 600 mg. in 5 days), and a similar group were given injections of saline. Except for a slight prolongation of fever in the cortisone-treated group there was no significant difference in the clinical course and incidence of complications in the two groups. One week after the onset of the infection the increase in the antistreptolysin titre was somewhat less in the sera of the cortisone-treated group than in the controls, but at 2, 3, and 4 weeks the formation of antibody was slightly greater in the cortisone-treated group than in the controls.

[The dose of cortisone employed is rather small. Larger doses or more prolonged administration might have different effects.]

*G. Ansell*

**TUBERCULOSIS**

**819. Pneumoperitoneum. (Pneumoperitoneum)**

O. K. THOMASSEN. *Nordisk Medicin* [Nord. Med.] 45, 127-129, Jan. 24, 1951.

Pneumoperitoneum as a treatment for pulmonary tuberculosis has been less used in Scandinavian than in a number of other countries. In 1947 it was adopted at Vensmoen Sanatorium in Norway for cases with cavities at the base of the lung (hilar level and below), for which it was felt that pneumothorax was inadequate and major surgery often disproportionately severe.

Of 44 patients, 34 who had been treated for at least 3 months were suitable for a preliminary analysis. The pneumoperitoneum was in all cases combined with either crushing or avulsion of the phrenic nerve. It was added to a pneumothorax in 11 and to a thoracoplasty in 2; in 21 it was the only form of treatment. In 10 patients the pneumoperitoneum was abandoned as ineffective. In 23 the cavities appeared to be closed, in 1 the cavity was reduced. Of the 23 successful cases, 16 patients have remained well for 2 years after discharge.

There appeared to be a relation between the degree of raising of the diaphragm and the success of the treatment.

The author concludes that pneumoperitoneum is a better treatment for low cavities than a pneumothorax, that is, it should be tried before resorting to major surgery in this type of case. In his series the results of pneumoperitoneum appeared to be better when there was not also a pneumothorax present.

*Margaret Agerholm*

**820. Relapse of Pulmonary Tuberculosis in Children following Sanatorium Treatment. (Les rechutes de la tuberculose pulmonaire chez l'enfant après une cure sanitaire)**

P. LOWYS and S. LENGRAND. *Archives de Médecine Sociale* [Arch. Méd. soc.] 7, 1-23, Jan.-Feb., 1951. 8 refs.

The authors define relapse as "any lymph-node, pleural, or pulmonary episode of tuberculous origin occurring not less than one year after the apparent cure or arrest of the patient's disease. Of 1,446 children treated in one sanatorium it was possible to get complete follow-up information on 1,021. The authors have analysed the incidence of relapse in these cases [they do not discuss reasons for absence of information on the remaining 425 cases, nor whether the incidence of relapse might have been more severe among those not followed up]. Relapse occurred in 73 of the cases studied. The authors give the age and sex distribution of the patients who relapsed, the length of their stay in the sanatorium, and the type of disease; 66 (90%) of these cases were pulmonary, whereas only 48% of all cases at the sanatorium were pulmonary; 52 had had collapse therapy. Within a year of leaving the sanatorium 64% were back to normal activity. Half the relapses occurred within the first 2 years, proof manifest [say the authors] of too rapid return to normal activity. In 58 cases the relapse occurred in summer and winter; in only 14 did it occur in spring or autumn. In 53 there were x-ray changes. In 71% of cases where bacteriological results were available they were positive. In cases initially unilateral half the relapses occurred in the other lung. The upper lobe was the most frequent site of relapse. At the time of reporting 17 patients had died of their relapse and 5 were deteriorating.

The authors study the factors which could be responsible for relapse. [Their analysis suffers from the fact that they give few particulars concerning the population of 1,021 patients among whom these 73 relapses occurred.] In 15 of 31 females the relapse occurred between the ages of 11 and 18, and in 31 of 45 males between the ages of 13 and 20; the authors conclude that puberty is therefore largely responsible. Among other factors incriminated are conditions of work, marriage, pregnancy, housing, psychological stress, and infectious diseases [but no comparable data are available for the cases that did not relapse].

*M. Daniels*

**821. Tuberculous Apical Fibrosis in Mass Chest Surveys. (Tuberkuløse toppfibroser)**

T. WESSEL. *Nordisk Medicin* [Nord. Med.] 45, 125-127, Jan. 24, 1951. 2 refs.

822. Follow-up of Tuberculosis Cases found by Mass Radiography 1945-6. (Etterkontroll av tuberkuløse funnet ved skjermfoto 1945-1946) P. CAPLAN. *Nordisk Medicin [Nord. Med.]* 45, 133-135, Jan. 24, 1951.

Mass radiography of all persons over 15 years of age was carried out in Trondhjem in 1945 and 1946. About 80% of the total population of 47,000 were examined. There were found 127 cases which required treatment (61 were negative for tuberculosis at the first examination) and 510 cases requiring observation. All the former and 362 of the latter patients were followed up for 5 years: 4 of the first group and 3 of the second group died of tuberculosis. In 36 of the first group and 31 of the second the disease showed progress in the radiographs. Fourteen of the first group and 9 of the second group were in hospitals or sanatoria; 84 of the first group (69%) were fit for work. The incompleteness of the follow-up of the second group makes their detailed analysis impossible.

The author comments on the increase in number of "good chronics" and emphasizes that their presence, often undiagnosed, in the community makes B.C.G. vaccination of increasing importance.

Margaret Agerholm

823. Tuberculous Pericarditis Treated with Streptomycin

A. FALK and R. V. EBERT. *Journal of the American Medical Association [J. Amer. med. Ass.]* 145, 310-314, Feb. 3, 1951. 14 refs.

The authors treated 27 patients who were suffering from tuberculous pericarditis and a proved pericardial effusion with 1 to 2 g. of streptomycin for 60 to 120 days. Circulatory failure disappeared in 8 patients, and in 7 there was no recurrence of failure during follow-up periods ranging between 5 and 24 months; the eighth patient died of tuberculous meningitis. The case fatality in the series was 35%; 4 other patients, 2 of them without evidence of pericardial effusion, were treated primarily by pericardectomy, with streptomycin therapy as adjuvant. In all 4 circulatory failure was relieved, and 3 returned to work. In none of them were there any post-operative complications due to tuberculosis.

W. G. Harding

824. Intermittent Streptomycin Regimens. An Analysis of Ninety-seven Patients with Pulmonary Tuberculosis Treated with One or Two Grams of Streptomycin Every Third Day

L. A. JAMES, L. J. SIDES, W. E. DYE, and V. F. DEYKE. *American Review of Tuberculosis [Amer. Rev. Tuberc.]* 63, 275-294, March, 1951. 5 figs., 17 refs.

To 97 patients (all males, 43 of whom were over 30 years of age) with pulmonary tuberculosis, 1 or 2 g. streptomycin was given every third day for 126 to 189 days. Of the 97 patients, 61 had far-advanced disease, 81 had evidence of cavitation, and 53 had old disease. Clinical evaluation at the end of 126 days of treatment showed improvement in 73 patients; this improvement usually occurred most rapidly during the first 42 days

of treatment. The commonest factors associated with poor clinical response were increased extent and chronicity of disease and, to a lesser degree, the development of bacterial resistance.

The incidence of toxicity was respectively 1.03% and 5.0% at the completion of 126- and 189-day courses. There were slight disturbances of vestibular function and minor erythematous rashes; 12 patients with endobronchial tuberculosis showed recession of their lesions in less than 126 days, mostly in the first 42 days of treatment. The greatest x-ray changes occurred during the first 84 days of therapy. At 126 days bacteriological "conversions" of at least 3 months' duration had occurred in 38% of patients. This compares favourably with a conversion rate of 19% in patients on a smaller daily dosage for a similar period. Furthermore, the incidence of drug-resistant tubercle bacilli in these patients was 31% compared with an incidence of 69% encountered in patients on a daily dosage schedule. Of the 81 patients with cavities, 18 of the 52 who continued to discharge tubercle bacilli were discharging drug-resistant organisms at 126 days, whereas of the 16 patients without cavities, only one of the 8 who remained "positive" was discharging drug resistant bacilli.

The authors [rightly] stress that the decreased incidence of streptomycin toxicity, delay in emergence of bacterial resistance, and the therapeutic efficacy of intermittent streptomycin regimens indicate the importance of determining the results of combining *p*-aminosalicylic acid and other anti-tuberculous drugs with intermittent dosage schedules.

Kenneth Marsh

825. Combined Intermittent Regimens Employing Streptomycin and *para*-Aminosalicylic Acid in the Treatment of Pulmonary Tuberculosis. A Comparison with Daily and Intermittent Dosage Schedules

C. W. TEMPEL, F. J. HUGHES, R. E. MARDIS, M. N. TOWBIN, and W. E. DYE. *American Review of Tuberculosis [Amer. Rev. Tuberc.]* 63, 295-311, March, 1951. 6 figs., 15 refs.

The authors treated 283 patients with pulmonary tuberculosis for 120 days as follows: 66 received streptomycin, 1 or 2 g. daily; 25 received *para*-aminosalicylic acid (PAS) 12 g. daily; 97 received streptomycin intermittently, 1 or 2 g. every third day; and 95 received streptomycin, 1 or 2 g. every third day, with 12 g. PAS daily. Care was taken to ensure that the groups were comparable as regards age, sex, and race; the duration, extent, and clinical types of the disease were also similar. The strains of tubercle bacilli isolated were sensitive *in vitro* to either streptomycin or PAS at the beginning of treatment.

Clinical response was found to be the same on all four schemes of treatment. Radiologically, the intermittent streptomycin-PAS regimen resulted in a higher incidence, and greater degree, of improvement. The incidence of sputum conversion was highest for the combined intermittent regimen. No instances of bacterial resistance have yet been encountered on this plan of treatment compared with 75.9% for daily streptomycin, 33.3% for

daily PAS, and 33.3% after intermittent streptomycin. A high incidence of toxicity (57%) on daily streptomycin decreased to 5% when the drug was given every third day. The incidence of toxicity for daily PAS was 5%, and 13% when the drugs were given together. The phenomenon of a loss of bacterial resistance to one or other of the drugs was encountered. This was marked in the daily PAS regimen.

From these observations it would seem that a combined intermittent course of streptomycin every third day and PAS daily is the treatment of choice for periods up to 4 months in non-miliary pulmonary tuberculosis.

*Kenneth Marsh*

**826. para-Aminosalicylic Acid (PAS) in Cavernous Pulmonary Tuberculosis. Oral Treatment. Comparison between the Effects of PAS in Oral and Transthoracic Administration. [In English]**

**H. DIFS.** *Acta Tuberculosis Scandinavica [Acta tuberc. scand.]* 25, 127-163, 1951. 6 figs., 31 refs.

A review is presented of 19 cases of progressive cavernous pulmonary tuberculosis treated with para-aminosalicylic acid (PAS) between 1945 and 1947. With one exception the patients received PAS orally in doses of 12 to 18 g. a day for periods of 1 to 7 months (on the average for 3 months). As a whole the results were very disappointing in this type of disease. Although in 10 cases a temporary improvement in the fever and/or in the erythrocyte sedimentation rate was observed, the cavities and the positive sputum persisted. Only one case with fresh exudative exacerbation showed radiological improvement: this, however, might have happened without chemotherapy. Two patients improved sufficiently to be able to undergo a thoracoplasty operation, but 1 died nevertheless 2 months after the operation. In no case was such improvement as might have been ascribed to the drug more than temporary. The author admits that the final course of the disease has not been influenced by the treatment in any of his cases.

The poor response to the treatment in this series is apparently due to the failure of the drug to reach the cavities, the main sources of bacilli, by the bloodstream in sufficient concentration. Inhalation of the drug from a nebulizer gave no better results. Direct injection of PAS through catheters inserted transthoracically into the cavities had a marked, though only transient, effect in the one case in which this method was employed as a last resort. However, even this patient died from further spread. The effect of bacteriostatic drugs depends on the drug reaching the focus of infection by the blood stream in adequate concentration. No serious side-effects of PAS were noticed.

[No mention is made of the effect of PAS on endobronchial tuberculosis. The poor results obtained in this series indicate that endobronchial lesions interfering with cavity drainage either did not play a decisive part in the disease process or, if present, such endobronchial lesions did not respond to the treatment sufficiently to influence the course of the disease.]

*E. G. W. Hoffstaedt*

**827. Clinical Observations on Automatic Endogenous Lymphadenobronchogenic Reinfestation in Pulmonary Tuberculosis of Adults. (Klinische Beobachtungen zur Frage der automatischen, endogenen, lymphadenobronchogenen Reinfektion bei der Lungentuberkulose Erwachsener)**

**G. NIGOGHOSSIAN and H. J. CRANZ.** *Acta Tuberculosis Scandinavica [Acta tuberc. scand.]* 25, 164-181, 1951. 28 figs., 47 refs.

A description and radiographs are given of 8 patients, aged 18 to 30, with lymphadenobronchogenic reinfection of pulmonary tuberculosis. This diagnosis was not established during the period of treatment of these patients: it is rather an "epicritical" interpretation of case histories selected in a review of 3 years' material in a 90-bed sanatorium. The suggested pathogenic mechanism is that of caseation and perforation of hilar lymph nodes into the adjacent bronchus, with subsequent "reinfection"-type phthisis. In none of these cases was the diagnosis confirmed by necropsy; bronchoscopy, which had been carried out in only 3 cases, was negative in 2 and showed caseo-necrotic endobronchitis with stenosis of the stem bronchus in 1 case. The evidence for the diagnosis rests on one or more of the following findings: the emergence of positive sputum following an acute exacerbation after a period with negative sputum; expectoration of caseous material; signs of atelectasis due to bronchial stenosis; radiological appearance of cavitation within a hilar lymph node. In some cases this cavitated lymph node—the indicator of the preceding perforation, as it were—is situated in the lung field at some distance from the hilum (para-hilar or peribronchial lymph node).

[The authors' argument is based on, and reinforced by, radiological and necropsy material reproduced from apparently similar cases, previously published. Though perhaps not all the radiographs which illustrate the series are so convincing that the diagnosis could in every case be accepted without reservation, there is, in conjunction with the reference made to Schwartz's cases, sufficient material collected to lend weight to the authors' suggestion. Re-infection adult tuberculosis may, perhaps more often than is usually accepted, be the consequence of perforation of a caseous hilar or peribronchial lymph node into a bronchus. In other words, cavernous phthisis may sometimes be a direct sequel of a tuberculous lymphadenitis.]

*E. G. W. Hoffstaedt*

**828. Lymphadenitis Tuberculosis Bronchostenotica. [In English]**

**K. ROGSTAD.** *Acta Tuberculosis Scandinavica [Acta tuberc. scand.]* 25, 305-325, 1951. 7 figs., 30 refs.

"Epituberculosis" is characterized by three negative features: absence of tubercle bacilli, absence of complicating caseous pneumonia, and absence of permanent radiological changes.

Biopsy, post-mortem, and tomographic findings of various authors (Rössle, Rich, Oppenheimer, Schwartz, and others) have, however, shown that the radiological opacity frequently found near the hilum in children is not just a transient "allergic" phenomenon as the

German originators of the term "epituberculosis" postulated.

Animal experiments as well as careful clinical examination employing tomography, bronchography, and bronchoscopy have revealed that the so-called perihilar or parahilar infiltration is primarily either a true pneumonic tuberculous infiltration or a fibrotic atelectasis—usually of the middle lobe. These pulmonary lesions are the direct or indirect consequence of tuberculous tracheo-bronchial or bronchopulmonary lymphadenitis. The enlarged lymph nodes either produce from without a compression bronchostenosis or, in case of necrosis, break down, rupture, and discharge their caseous content into the adjacent bronchus. Thus the bronchus is either blocked and infected—endobronchial tuberculosis thus producing bronchostenosis from within—or tuberculous aspiration pneumonia results. Bronchostenosis usually leads to either bronchiectasis or atelectasis—or both. At the same time compensatory emphysema (or, in cases of valve action, obstructive emphysema) ensues which often masks the atelectatic collapse of the middle lobe on a plain postero-anterior radiograph.

The perihilar infiltration as seen on an ordinary chest film may be due to any of the following conditions: (1) density (infiltration or atelectasis) of the apical segment of the lower lobe; (2) density of the middle lobe; (3) density of posterior or anterior segment of the upper lobe; (4) early manifestation of an interlobar pleural effusion (due to perforation of a caseous lymph node into the interlobar pleural space): this can be demonstrated on films taken in the lordotic position; and (5) very occasionally a genuine "tuberculo-toxic perifocal exudate" (perihilar infiltration proper). Lateral and oblique plain and tomographic radiographs are required in order to establish a correct diagnosis. Bronchoscopy, though often showing tenacious pus with scanty tubercle bacilli (if any) sometimes fails to demonstrate the bronchial stenosis which might be situated beyond the visible ostium of a lobar bronchus. Here tomography usually clinches the diagnosis. Obstructive emphysema as a result of bronchostenosis with valve action (similar to the mechanism of tension cavities) is often missed, though the expiratory mediastinal shift to the contralateral side (Holzknecht-Jacobsohn phenomenon) is pathognomonic in the absence of pneumothorax.

Although the bronchostenotic atelectasis does not necessarily show on a routine film and although the remaining bronchiectasis in children may be symptomless, the old concept of "epituberculosis" ought to be abandoned. The author offers instead the term: "lymphadenitis tuberculosa bronchostenotica" or the "bronchial lymph-node syndrome in children". As this condition is usually benign—in children, at least—and as, on the other hand, caseous and partly calcified lymph nodes would not yield to any antibiotic, chemotherapy has never been attempted in these children. It is, however, stressed that in the majority of the 26 cases described in this paper tubercle bacilli could be found eventually, sometimes in gastric washings. It appears, therefore, desirable to establish the correct diagnosis of the syndrome at an early stage, possibly before the develop-

ment of necrosis, when intensive chemotherapy might possibly control the infection at the source—therapia magna sterilans.

[The corollary of this therapeutic concept is to subject every child in whom tuberculous nodes—hilar or other—have been diagnosed without any other demonstrable active tuberculous lesion to a full course of streptomycin or other chemotherapy; or alternatively to excise all visible or palpable lymph nodes surgically. The therapeutic enthusiasts must be careful not to pour out the baby with the bath.]

E. G. W. Hoffstaedt

#### 829. Resistance of *Mycobacterium tuberculosis* to Chemotherapeutic Agents

W. H. BAILEY. *American Journal of Clinical Pathology* [Amer. J. clin. Path.] 21, 241-246, March, 1951.

Over 1,000 smears and cultures of *Mycobacterium tuberculosis* were studied from a series of 320 consecutive patients with tuberculosis who were treated with streptomycin, dihydrostreptomycin, *p*-aminosalicylic acid (PAS), or thiacetazone. Resistance to streptomycin and dihydrostreptomycin developed in the tubercle bacilli in 102 patients (31.8%). Of a series of 278 patients receiving streptomycin, organisms from 65 (23.3%) developed a definite resistance to a concentration of 10  $\mu$ g. streptomycin per ml. of medium. All 65 of these patients were later given a course of PAS, alone or in combination with streptomycin: 10 (15.3%) of the resistant cases showed an appreciable lessening of their resistance to streptomycin rather promptly after beginning PAS. No appreciable resistance to PAS alone was found.

Kenneth Marsh

#### 830. The Therapeutic Effect on Experimental Tuberculosis in Guinea Pigs of 4-Acetylaminobenzal Thiosemicarbazone (Tibione) in Combination with Dihydrostreptomycin as Compared with the Effect of *para*-Aminosalicylic Acid in Combination with Dihydrostreptomycin

D. M. SPAIN and W. G. CHILDRESS. *American Review of Tuberculosis* [Amer. Rev. Tuberc.] 63, 339-345, March, 1951. 6 figs., 5 refs.

In guinea-pigs it was found that thiacetazone ("tibione") (50 mg.) in combination with a sub-effective dose of dihydrostreptomycin (2 mg.) was more effective as an anti-tuberculous agent than the combination of *p*-aminosalicylic acid (100 mg.) with a similar dose of dihydrostreptomycin. The former combination was also more effective than thiacetazone alone.

Kenneth Marsh

#### 831. Blood Volume and Extracellular Fluid in Tuberculosis

E. B. HAY, C. R. HAY, and D. E. JENKINS. *Journal of Thoracic Surgery* [J. Thorac. Surg.] 21, 42-47, Jan., 1951. 3 figs., 17 refs.

In patients with tuberculosis studied there was a reduction in red cell mass, an increase in plasma volume, an increase in extracellular fluid (thiocyanate space), and reduced serum total protein and serum albumin,

when compared to the healthy adults. These changes were more marked in those patients who were considered to be in poor condition, by the criteria used.—[Authors' summary.]

**832. Studies of the Cerebrospinal Fluid Circulation in Tuberculous Meningitis in Children. Part I. The Use of Penicillin as a Tracer Substance. Part II. A Review of 100 Pneumoencephalograms**

J. LORBER. *Archives of Disease in Childhood [Arch. Dis. Childh.]* 25, 404-409, Dec., 1950, and 26, 28-44, Feb., 1951. 19 figs., bibliography.

In order to note the rapidity with which penicillin or streptomycin reached various levels of the cerebrospinal pathway, 15,000 units of penicillin was injected, usually by the lumbar but occasionally by the cisternal or ventricular routes, and an assay was made in the fluid removed by cisternal or ventricular puncture 5 or 10 minutes later. It was felt that this short space of time would not allow of absorption of the penicillin into the blood stream or of its resecretion into the fluid. In the absence of block, diffusion of penicillin took place rapidly irrespective of the site of its injection, a fact which, the author claims, strengthens the suggestion that there is not only an outward flow from the ventricles but an active circulation of the fluid.

For the precise determination of the site of block the method proved inferior to air studies. It was found, for instance, that penicillin assay was unsuitable for the determination of block at the tentorial opening because of the difficulty, and sometimes impossibility, of obtaining fluid from the cerebrospinal fluid over the surface of the brain. Because of the possibility of being able to institute treatment early, the greatest practical importance of penicillin assay lay in the detection of spinal blocks which were not necessarily permanent. Spinal block was suspected in 20 cases, proved in 12, and disproved in 8.

The author holds that in the absence of a block there is no merit in administering streptomycin except by the lumbar route. Tentorial block, or the hydrocephalus due to it, does not necessitate ventricular or cisternal injection, because there is still free communication between the lateral ventricles and the lumbar theca.

The results are analysed of 100 pneumoencephalograms taken from 58 children with tuberculous meningitis (bacteriologically confirmed in 57). The examination was well tolerated, especially if they spent 3 hours subsequently in an oxygen tent—a procedure known to hasten the absorption of the injected air. Moderate headache and some vomiting for the first 24 hours were fairly frequent. Much information could be obtained after the injection of as little as 5 to 10 ml. of air if the films were taken in the upright position. Encephalography was preferred to ventriculography unless the former was contraindicated by reason of papilloedema or the ventricles failed to fill because of obstruction of the pathways. In no case was there evidence of relapse within 2 months of examination, although a considerable pleocytosis might be provoked in the fluid.

Of 22 children who presented normal encephalograms, 18 did so between the fourth and fourteenth month after the beginning of treatment. The 36 in whom abnormalities were found included 6 whose first examination proved to be normal. Abnormalities were usually: (1) the presence of more than one block in the cerebrospinal pathways; (2) absence of air in the subarachnoid space; and (3) hydrocephalus. One or more blocks other than in the cord were found in 30 cases, invariably at the tentorial opening or in the basal cisterns. Aque ductal blocks were found additionally in two instances, and obstruction of the fourth-ventricle foramina in three. As the absence of subarachnoid air (to be distinguished from subdural air, which may appear in any encephalogram) was noted in all cases of tentorial or basal cisternal block, great importance is attached to it as a sign; it preceded the hydrocephalus in 3 cases. Hydrocephalus occurred in 34 cases in all.

As was to be expected a close correlation was found between pneumoencephalographic appearances and prognosis. There was, however, no correlation between the encephalographic findings and the subsequent mental development of children surviving the infection. Encephalography, says the author, may supply criteria for the selection of cases for treatment and for the abandonment of treatment on humanitarian grounds.

W. H. McMenemey

**833. Tuberculous Meningitis in Children Treated with Combined Streptomycin and Potassium Iodide**

F. T. ROQUE and E. A. CLEVE. *Diseases of the Chest [Dis. Chest]* 19, 319-324, March, 1951. 4 refs.

**834. An Involuntary Clinical Experiment on the Resistance of Children Vaccinated with Anatuberculin (Salvioli's Method) and Unvaccinated Children Exposed to a Highly Infectious Source; Second Communication. (Esperimento clinico, involontario, sulla resistenza di bambini vaccinati (V.P.S.) e non vaccinati contro la T.B.C. di fronte a contagio altamente infettante. Nota 2)**

A FERRO and S. TARONNA. *Clinica Pediatrica [Clin. pediat., Bologna]* 33, 1-22, Jan., 1951. 21 figs.

An account of this outbreak has already been published (see *Abstracts of World Medicine*, 1950, 8, 554), and the authors now give more details, partly in reply to points raised by readers of their first paper: a third paper on the incident is promised. It is made clear that (a) the whole building at Dolo, including the second floor, had previously been used for cases of tuberculosis; (b) breast-fed infants had been kept on the first floor, with those already weaned, opposite the x-ray rooms for the first 3 months, at the end of which a dormitory for breast-fed infants was provided on the second; floor (c) all infants were transferred to the first floor when 1 year old. All the nursing staff, nuns as well as lay nurses, were medically examined and x-rayed at the onset of the outbreak and none was found infected. The outbreak set in simultaneously on both floors. Vaccinated and unvaccinated children mixed freely together. All milk was heat-treated in a water-bath for 20 minutes. There was no evidence to suggest abdominal

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or bone tuberculosis. This paper gives further x-ray and other individual details of the affected or suspected cases. The case incidence worked out at 16.6% among the children who had been vaccinated and 26.9% among the unvaccinated. Whereas 57.1% of the latter group showed exudative lesions, none was found among those who had been vaccinated.

J. Cauchi

**835. Duration of B.C.G. Allergy. (BCG-allergiens variguet)**

T. GEDDE-DAHL. *Nordisk Medicin [Nord. Med.]* **45**, 122-123, Jan. 24, 1951. 5 figs.

By the end of 1949, 826 of the 3,000 employees of the Telephone Service of Oslo had been vaccinated with B.C.G., most of them for the first time, some time during the previous 3 years. All cases were re-tested (Pirquet with adrenaline, and Mantoux 1 mg.) 3 months after the initial vaccination and then once a year. Re-vaccination was carried out where necessary.

By the end of 1949 the proportion showing an attenuated allergic reaction was rather large: about one-third had had 1, and 7% 2 re-vaccinations; 4 patients (0.7%) developed clinical tuberculosis. One developed the disease in the anti-allergic phase 6 weeks after vaccination and a few days after giving a weakly positive Pirquet reaction; 2 who were Pirquet-negative after vaccination developed the disease respectively 1 and 5 years after vaccination; the fourth patient had been vaccinated 4 years previously and the Pirquet test had been positive for 2 years, and the Mantoux test weakly positive for 6 months.

The author stresses the importance of follow-up tuberculin tests. Slight allergy may not be a sufficient protection, and a positive Pirquet reaction is significant.

Margaret Agerholm

**836. The Fluctuation of the Tuberculin Reaction in Different Geographic Areas and its Relationship to Resistance**

J. D. ARONSON. *American Review of Tuberculosis [Amer. Rev. Tuberc.]* **63**, 121-139, Feb., 1951. Bibliography.

A further report dealing with fluctuations in the tuberculin reaction is based on the author's well-known studies on tuberculosis among North American Indians. The reactions to doses of 0.00002 mg. and 0.0005 mg. tuberculin P.P.D. among a control group of 1,432 persons and a B.C.G.-vaccinated group of 1,541 persons living in Arizona, Wyoming, North and South Dakota, and Alaska, observed over a period of 9 to 11 years, were classified into 10 categories. Persistent high sensitivity to tuberculin was more frequent among the controls than the vaccinated. Reversion to negative or decrease in sensitivity occurred more often in vaccinated persons. In areas where there was a high incidence of tuberculosis, increase in tuberculin-sensitivity, suggesting superinfection, took place in the B.C.G.-vaccinated groups. Fluctuations in the level of sensitivity and reversion to negative occurred with greatest frequency in the group living in Arizona, and it is suggested that this might have been due to climatic factors, particularly exposure to sunlight.

J. E. M. Whitehead

**837. Spondylitis Tuberculosa and its Relation to Neurological Affections. [In English]**

A. C. DE VET. *Archivum Chirurgicum Neerlandicum [Arch. chir. neerl.]* **2**, 303-325, 1950. 5 figs., 45 refs.

The author, at the Neurosurgical Clinic, Wassenaar, reviews 35 cases of tuberculous spondylitis. He points out that a neurosurgeon will see transverse cord lesions due to tuberculous vertebral disease quite often before a diagnosis of tuberculosis has been made, whereas the tuberculosis specialist watches the cord lesion develop in the patient already diagnosed as tuberculous. He quotes extensively from the work of others, notably Sorrel-Déjérine (*Contribution à l'étude des paraplégies Pottiques*, Paris, 1926).

He attempts to classify the stages of the illness and the need for operation thus: (1) Those cases of tuberculous spondylitis developing a transverse lesion at an early stage while undergoing treatment usually undergo spontaneous cure and rarely require operation. (2) Those developing after a year of treatment may require operation. (3) Those where the diagnosis of tuberculous spondylitis is made when the patient is being examined for an initial neurological lesion should not be subjected to operation. (4) It is possible to find epidural tuberculosis without spondylitis.

The author warns against misdiagnosing these neurological lesions as due to disk herniation, for the result is likely to be fatal if the patient is subjected to operation. Tomography may be a valuable aid in diagnosis. If a decompression operation is undertaken it should be a ventral decompression according to the technique of Alexander and Dott. Laminectomy does not relieve pressure adequately; it merely weakens further the bony spinal column. Streptomycin is a valuable aid as a chemotherapeutic cover during operation.

Elliot E. Philipp

**838. The Effect of Adrenocorticotropic Hormone (ACTH) on Experimental Tuberculosis in Mice. Preliminary Report. [In English]**

B. SWEDBERG, G. DAHLSTRÖM, and R. LUFT. *Acta Endocrinologica (Copenhagen) [Acta endocrinol., Kbh.]* **6**, 215-220, 1951. 2 refs.

See also Sections Pharmacology and Therapeutics, Abstracts 499, 500, and 509; and Microbiology, Abstracts 581, 583, and 593.

**TYPHOID FEVER**

**839. Treatment of Typhoid Fever with Terramycin**

W. A. REILLY and A. M. EARLE. *Journal of Pediatrics [J. Pediat.]* **38**, 428-430, April, 1951. 3 refs.

From the Pediatric Department, University of Arkansas, the authors report on the effective treatment of 4 out of 6 patients suffering from typhoid fever with terramycin. Dosage was from 2 to 3 g. daily, divided into equal doses given 6-hourly. The drug was administered orally either in capsules or in an elixir. In 4 cases there was a good clinical response, all the

symptoms subsiding within 4 days. There were no sequelae or relapses, nor did the carrier state develop up to 3 months from the date of discharge from hospital. In the 2 cases which failed to respond it is considered that dosage may have been inadequate. No toxic effects were observed to follow terramycin in the dosage prescribed. The authors remark that since terramycin is relatively non-toxic the dose of from 2 to 3 g. daily could be increased to deal with severe infections. They recommend doses of 200 mg. per kg. daily in the worst cases. It is not at present possible to assess the relative merits of terramycin and chloramphenicol in the treatment of typhoid fever.

Joseph Ellison

840. An Epidemic of Typhoid Fever with 156 Cases, Mostly Treated with Chloramphenicol. (Über eine Typhusepidemie mit 156 Erkrankungen, vorwiegend behandelt mit Chloromycetin)

F. BECKERMANN and G. OTTO. *Deutsche Medizinische Wochenschrift* [Dtsch. med. Wschr.] 76, 466-470, April 6, 1951. 3 figs.

A typhoid endemic in a children's home on a North Sea island is described; there were 156 cases, among them 114 children up to the age of 16 years. Over 80% of those affected were treated with chloramphenicol. This treatment is discussed in detail; the dosage scheme adopted was 60 to 100 mg. per day for children and 60 mg. for adults per kg., divided into 4 doses. After the temperature had fallen to normal the dosage was halved, and subsequently reduced to 1 g. per day (0.75 g. for children).

The results were extremely favourable, one child only died, there were no cases of intestinal perforation, and only 5 (3.2%) of intestinal haemorrhage, all of them mild. Circulatory collapse occurred in 12 cases, and the likelihood of its causation through the sudden liberation of bacterial endotoxins is again stressed. Relapse occurred in no less than 44% of the cases treated with chloramphenicol, but responded promptly to renewed medication with this drug. The authors therefore recommend that treatment be continued for a full fortnight after the temperature returns to normal.

W. G. Harding

841. Treatment of Typhoid Fever. I. Combined Therapy with Cortisone and Chloramphenicol

J. E. SMADEL, H. L. LEY, and F. H. DIERCKS. *Annals of Internal Medicine* [Ann. intern. Med.] 34, 1-9, Jan., 1951. 1 fig., 15 refs.

To 8 patients with typhoid fever chloramphenicol and cortisone were given in the following dosage: chloramphenicol, an initial dose of 3.0 g., followed by 1.5 g. 12-hourly on 9 occasions, followed by 1.5 g. daily for 10 to 11 days; cortisone: (a) an initial dose of 200 mg. during the first 24 hours followed by 100 mg. on each of 3 days; or (b) 300 mg. on the first day, 200 mg. on the second day, and 100 mg. on the third and fourth days. Previous experience with chloramphenicol alone in the treatment of typhoid fever had shown that on the average 4 days elapsed between the start of treatment and an obvious diminution of toxæmia and subsidence of fever.

The 8 patients studied could be divided into 2 groups of 4, the first of which received the lower dose of cortisone, the second the higher dose. In the first group the average duration of fever after the beginning of treatment was 50.2 hours. In the second group the average duration of fever was 15.5 hours. In the group receiving the larger dose of cortisone the effect of the combined therapy was sometimes startling; in 24 hours each of the patients was afebrile, and 3 were sitting up in bed and were so bright and cheerful that they seemed almost euphoric. The response in those patients who received the smaller dose of cortisone was not so dramatic, and relapse occurred in 2 cases.

Discussing their results the authors draw attention to the danger of regarding the feeling of well-being noted in their patients as a sound criterion for estimating the adequacy of treatment. Obviously the hazard of intestinal perforation may not disappear as promptly as the fever. Commenting on the mode of action of cortisone they speculate that this may result from some beneficial action on the host's reaction to his infection, rather than on the typhoid organism or its products.

[As one would expect, this is a carefully compiled paper that should be read in the original by those who are interested in the subject.]

T. Anderson

842. Treatment of Typhoid Fever. II. Control of Clinical Manifestations with Cortisone

T. E. WOODWARD, H. E. HALL, R. DIAS-RIVERA, J. A. HIGHTOWER, E. MARTINEZ, and R. T. PARKER. *Annals of Internal Medicine* [Ann. intern. Med.] 34, 10-19, Jan., 1951. 4 figs., 9 refs.

Cortisone alone was given in the treatment of 7 proven cases of typhoid fever, the dose, administered intramuscularly, being for adults 200 to 300 mg. in the first 24 hours, 200 mg. on the second day, and 100 mg. on the third day. Clinical improvement was observed in the first 36 hours, and in 6 patients the temperature had also subsided within this time. In one patient only was chloramphenicol required in the initial phase. The initial blood culture was positive in 6 of the 7 patients; in 3 it was negative 24 hours later and in the other 3 patients it became negative on the 2nd, 4th, and 5th days respectively. There was no obvious effect on the stool culture. One patient had a relapse, but responded rapidly to chloramphenicol: in another, first seen late in the disease, haemorrhage occurred, but the bleeding was not excessive and recovery followed. Illustrative records of 4 cases are given. In 4 further cases treated with chloramphenicol as well as cortisone rapid amelioration was observed in 12 to 48 hours.

[These results (and those reported in Abstract 841) are of obvious importance and re-direct our attention to the value of the host response in recovery from an acute infection.]

T. Anderson

843. Results Obtained with a Glycerolated Vi Antigen in the Detection of Chronic Typhoid Carriers

M. SAINT-MARTIN and J. M. DESRANLEAU. *American Journal of Public Health* [Amer. J. publ. Hlth] 41, 687-692, June, 1951. 22 refs.

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## PROTOZOAL INFECTIONS

844. Development of Arizona *Trypanosoma cruzi* in Mouse Muscle

S. F. WOOD. *American Journal of Tropical Medicine [Amer. J. trop. Med.]* 31, 1-11, Jan., 1951. 36 figs., 14 refs.

According to some authors, in the course of development of *Trypanosoma cruzi* in the muscles of its vertebrate host there is an intermediate crithidial stage between the leishmanial and trypanosomal stages. However, the present author, who has studied the development of Arizona strains of *T. cruzi* in white mice infected by intramuscular inoculation of droppings from naturally infected triatomid bugs (*Triatoma protracta* and *T. rubida uhleri*), failed to find any crithidial forms among upwards of 5,000 parasites examined in impression smears of the muscle tissues stained by the Jenner-Giemsa method.

A detailed illustrated account is given of the transformation of the leishmanial forms into trypanosomes, which may proceed directly or indirectly. In the direct process the rounded parasite first acquires a flagellum, which gradually increases in length, pulling the body with it, until the latter elongates and assumes the characteristic trypanosome form. In the indirect process the growing flagellum adheres to the surface of the rounded body and gradually encircles it, reaching the region of the kinetoplast. At this stage a V-shaped indentation is formed in the body between the free anterior end of the flagellum and the kinetoplast area. As the indentation deepens, the anterior end of the body (with the free flagellum) separates from the posterior end (kinetoplast area), until finally the flagellate unfolds and assumes the trypanosome form. The author has found no evidence of the formation of the trypanosome form by migration of the kinetoplast. *C. A. Hoare*

## 845. The Effect of Endochin on Experimental Toxoplasmosis

W. D. GINGRICH and E. M. DARROW. *American Journal of Tropical Medicine [Amer. J. trop. Med.]* 31, 12-17, Jan., 1951. 9 refs.

Since *Toxoplasma* is an obligatory tissue parasite with a predilection for the reticulo-endothelial system, it was thought that this parasite might respond to anti-malarial drugs which are active against the exoerythrocytic stages of *Plasmodium*. Tests were accordingly carried out with experimentally infected canaries and mice, using sulphonamides (sulphadiazine), "metachloridine", sulphones ("promin"), naphthoquinones, 8-aminoquinolines (pentaquine), biguanides (proguanil), and acridone derivatives ("endochin"). In birds, the drugs were given by mouth 2 to 3 times daily for 5 days. Endochin (0.3 to 0.4 g. per kg. daily) and sulphadiazine (2.5 to 3.3 g. per kg.) were the only drugs which delayed the death of the infected birds beyond that of the control group: 8.6 days in the case of the former, and 10 days in the case of the latter. The same compounds, as well as another acridone derivative, were tested on infected young mice, some of which received with their

diet a 1% mixture of the acridones and 0.5% mixture of sulphadiazine immediately after infection, and others after 3.5 days. The respective daily doses were 0.8 to 1.2 g. per kg. and 0.4 to 0.6 g. per kg. for sulphadiazine, and 1.9 to 2.9 g. per kg. and 0.6 to 0.9 g. per kg. for endochin. These 2 drugs also had a delaying effect on the course of the disease, whereas the second acridone was without effect.

Experiments were then made to see if there was any summation or potentiation of the effects of sulphadiazine and endochin. The drugs, singly or combined, were given to infected mice immediately for 5 days in one group, for 15 days in another, and starting on the sixth day after inoculation for 10 days in a third group. The survival period was greatest in the second group (immediate long-term treatment), within which the sulphadiazine-treated mice survived longer. However, there was no evidence of a summation effect, since combined treatment was less effective than sulphadiazine alone in the first and second groups, but more effective in the third group. The examination of various tissues of the survivors revealed no parasites, while the subinoculation of ground tissue suspensions into clean mice failed to infect them.

In a final experiment, infected mice underwent courses of immediate (up to 5th day) or delayed (6th to 15th day) treatment with promin (daily doses 1.8 and 0.6 g. per kg. respectively). Six animals survived immediate treatment and, when killed, their tissues showed no parasites and failed to infect clean mice. The tissues of the survivor of delayed treatment produced a fatal infection when subinoculated, and pseudocysts were found in sections of its brain.

*C. A. Hoare*

## 846. Aureomycin Treatment of Acute Experimental Toxoplasmosis in Rabbits. [In English]

E. KASS and E. STEEN. *Acta Pathologica et Microbiologica Scandinavica [Acta path. microbiol. scand.]* 28, 165-168, 1951. 1 fig., 5 refs.

Rabbits were inoculated intraperitoneally with peritoneal exudate from mice infected with *Toxoplasma gondii*, penicillin (175 units per ml.) and streptomycin (2,800 units per ml.) being added to prevent contamination. Six animals were given 20 mg. aureomycin intramuscularly three times daily, starting 2 hours before inoculation with *Toxoplasma* and continuing so long as the animals had fever; 6 animals were retained as untreated controls.

Of the control group 5 animals died: moreover, the survivor had been inoculated with very few organisms. Of the test animals, only 1 died. Sera from the survivors gave strongly positive reactions to complement-fixation dye tests.

*R. B. Lucas*

## 847. Sontoquine Naphthoate in Amebiasis

N. J. CONAN. *American Journal of Tropical Medicine [Amer. J. trop. Med.]* 31, 18-19, Jan., 1951. 9 refs.

"Sontoquine" is a 4-aminoquinoline derivative possessing similar antimalarial properties to chloroquine. The naphthoate salt was selected for trial because of its

poorer absorption, yielding double the faecal concentration of the bisulphate salt. Of 6 patients with amoebiasis and positive stools who were given 0.3 g. of sontoquine naphthoate base daily for 14 days, 3 continued to pass amoebae in the faeces after treatment; amoebae were not found in the other 3 during an observation period of 5 months. One of the latter group had hepatitis which subsided under treatment within 3 to 4 days. It is concluded that sontoquine acts similarly to chloroquine, being good in hepatic and poor in intestinal infections. The theoretical advantages due to the poorer absorption of the naphthoate salt are not apparent in practice.

J. L. Markson

See also Section Pharmacology and Therapeutics, Abstract 501.

**848. The Correlation between Blackwater Fever, Malaria, Quinine and Atebrin**

H. FOY and A. KONDI. *Annals of Tropical Medicine and Parasitology* [Ann. trop. Med. Parasit.] 44, 309-318, Dec., 1950. 4 figs., 32 refs.

Evidence is presented to show that in Greece the incidence of blackwater fever in the past has been directly related to the volume of malaria in the same year and that there is a significant degree of correlation between the taking of quinine and the appearance of the symptoms. The use of quinine by the peasant population had been sporadic and insufficient, and usually only in treatment of attacks of malaria; this in itself may have been one of the factors leading to the high incidence of blackwater fever. During the war years, quinine became unobtainable and was replaced by mepacrine. The taking of mepacrine in the same manner would be expected to be much more effective, especially in *Plasmodium falciparum* infections: it is generally assumed that this parasite is intimately concerned with the genesis of blackwater fever. Enemy occupation and the breakdown of organized life led in 1942 to a major epidemic of malaria, but the hospital records in Salonika show that this was not followed by a corresponding increase in the number of cases of blackwater fever. The substitution of mepacrine for quinine is thought by the authors to have played a major part in this decrease and also in the fall in the number of cases of malaria in the years following 1942.

Of 106 patients with general paralysis of the insane who were inoculated with blood from 58 cases of blackwater fever, not one developed blackwater fever, although most developed malaria.

I. M. Rollo

**849. "Sontochin" ("Nivaquine") and its Therapeutic Action in Malaria.** (Sontochin (Nivaquine) in seiner therapeutischen Wirkung bei Malaria)

W. MENK and W. MOHR. *Zeitschrift für Tropenmedizin und Parasitologie* [Z. Tropenmed. Parasit.] 2, 351-361, Jan., 1951. 7 figs., 7 refs.

"Sontochin" was given in 1,100 cases of malaria, including 978 cases of vivax, 9 of quartan, and 121 of falciparum infection, with good results. The toxic effects were slight, even with large doses: a slight fall

in the blood pressure was noted after intravenous administration, but the general effects on the circulation were negligible. Excretion was not very rapid and the drug was detectable in the urine for about a week after cessation of dosage.

The dosage recommended varies with the severity of the disease and the species of infecting plasmodium. For slight falciparum infections the dosage recommended is: orally, 0.3 g. twice a day for one week, together with pamaquin, 0.01 g. twice a day for 3 days or followed by pamaquin, 0.01 g. three times a day for 3 days. For severe infections sontoquin is given intravenously, 0.2 g. twice or three times a day on the first day, for the next 1 or 2 days also intramuscularly, 0.15 to 0.2 g. once or twice a day, to be followed by oral sontoquin with pamaquin for a week. Vivax infections were treated with a total of 2 to 2.5 g., together with pamaquin (as above). Relapses were not prevented by this medication, but on the dosage recommended methaemoglobinæmia did not develop.

The claim is made that sontoquin acts rather more rapidly than mepacrine [though this is hardly borne out by the temperature charts given].

W. H. Horner Andrews

**850. The Results of DDT Spraying in French Guiana: Destruction of *Aedes aegypti* and Spectacular Reduction in the Incidence of Malaria.** (Les résultats de la "défécitisation" en Guyane française: destruction de *Aedes aegypti*, et réduction spectaculaire du paludisme)

H. FLOCH. *Revue du Paludisme* [Rev. Palud.] 9, 49-57, March 15, 1951. 2 figs.

After a campaign of spraying with DDT in French Guiana lasting 2 years, the main aims of the programme, namely, the eradication of *Aedes aegypti*, vector for yellow fever, and the suppression of *Anopheles darlingi*, malarial vector, have been achieved.

In particular, *A. aegypti* had completely disappeared from Cayenne (containing nearly half the total population of the colony) by the end of the first year and from the whole of the coastal area by the end of the second; *A. aegypti* has in fact been eradicated from the colony; *A. darlingi* no longer exists in Cayenne. The importance of this last achievement is shown by the fall in the number of cases of malaria, which started in February of the second year. This fall was maintained and accentuated during June and July, when the annual epidemic of malaria usually starts. The total number of cases had fallen by 74% from February to August when compared with the average for the preceding 3 years.

The only toxic effects, dermatitis of the wrists and forearms, were produced by the petroleum in which the DDT was dissolved (a 5% solution), but a suspension of wettable DDT in water was later used.

Possible DDT resistance has developed in *Culex fatigans*, 11% of which were found to carry microfilaria of *W. bancrofti*, and in *Musca domestica*. "Gammexane" sprays will be used to deal with this problem.

I. M. Rollo

See also Section Microbiology, Abstracts 589-91.

# History of Medicine

## 851. Leonardo da Vinci, and the Movement of the Heart

K. D. KEELE. *Proceedings of the Royal Society of Medicine* [Proc. R. Soc. Med.] 44, 209-213, March, 1951. 3 figs., 4 refs.

Of the 5,000 pages of Leonardo da Vinci's known manuscripts about 190 are on anatomical subjects, and of these about 50 deal with the heart. The present author offers a brief but interesting synopsis of these pages and seeks to assess Leonardo's real views on cardiac function. His basically Galenic background is reviewed and its rational modifications noted. Leonardo believed that the essential function of the heart was to produce heat by churning the blood. The heat, combined with "natural gravity", caused the blood to travel from the heart to the periphery. No Harveian conception of true circulation is revealed.

Leonardo's contributions to the knowledge of anatomy are described, including his accurate account of the four chambers, the coronary vessels, the papillary muscles, and the valves. He speculated on the nature of arteriosclerosis and of a patent foramen in the interatrial septum. Three of Leonardo's annotated drawings are reproduced, and some description of his methods of investigation is given. These included the making of wax casts of bullocks' hearts, inflating the lungs with bellows, and distending the ligated heart.

[The author states his intention to produce in book form a full account of Leonardo's work on the heart. The present article raises the hope that this will not be too long delayed.]

Calvin P. B. Wells

## 852. The Repair of Nerves by Suture

W. HOLMES. *Journal of the History of Medicine and Allied Sciences* [J. Hist. Med.] 6, 44-63, Winter, 1951. Bibliography.

Galen was probably the first to demonstrate that a breach in the continuity of a nerve was followed by loss of sensation or of motion in the area supplied by the nerve. But in Galen's day, and for centuries afterwards, it was believed that no treatment could restore the function after a nerve had been completely divided. It is true that even as early as the fourteenth century the suture of nerves was undertaken by Guy de Chauliac and other surgeons, but although Paré in the sixteenth century and Richard Wiseman in the seventeenth each described the effects of nerve injury, neither of them suggested treatment by suture.

The modern period opened in 1776, when William Cumberland Cruikshank, who assisted the Hunters in the teaching of anatomy, performed his experiment on nerve regeneration in the dog, although his work remained unpublished for 19 years. Meanwhile, Abbé Felice Fontana of Pisa, who had discussed the matter with Cruikshank in London, confirmed his conclusions after similar experiments. Another visitor to London,

Arnemann of Göttingen, also repeated the experiments but opposed Cruikshank's claims, while another whose results were negative was C. F. Michaelis of Cassel. The general tendency early in the nineteenth century was to discount the possibility of nerve regeneration, but the problem was far from settled. Prévost in 1826, Flourens in 1828, and Tiedemann in 1831 each produced evidence to show that a divided nerve might regenerate. In 1864 it was claimed on behalf of Nélaton that he had sutured a divided median nerve and that sensation and motion were restored in 7 days. James Paget, in 1853, had even suggested that a rapid return of function might follow the healing of a divided nerve "by first intention". For a while this was regarded as possible, and although Waller in 1850 had suggested that the distal segment underwent degeneration and that regeneration was the result of the downgrowth of fibres from the intact proximal end, it took a long time for the peripheral theory of regeneration to be disproved. But gradually the outgrowth theory of regeneration and the belief in the value of nerve suture received support from such authorities as His and Cajal. In 1892-3 Howell and Huber, in a scholarly essay which won the prize offered by the American Physiological Society for the best research on the subject, showed by reference to decisive experiments and by a review of published cases of nerve suture in man that the repair of nerves by suture was a procedure fully justified by the results.

[There are 52 references in this clear and excellent account of the subject.]

Douglas Guthrie

## 853. Goethe and the Physicians

K. A. BAER. *Bulletin of the History of Medicine* [Bull. Hist. Med.] 25, 159-168, March-April, 1951. 2 figs.

## 854. Resurrection Riots during the Heroic Age of Anatomy in America

L. F. EDWARDS. *Bulletin of the History of Medicine* [Bull. Hist. Med.] 25, 178-184, March-April, 1951.

## 855. François Magendie (October 6, 1783-October 7, 1855)

P. F. FENTON. *Journal of Nutrition* [J. Nutrit.] 43, 3-15, Jan. 10, 1951. 1 fig., 8 refs.

The life of François Magendie must be considered against the background of political and intellectual upheaval which characterized his era. He was a child of the French Revolution and followed the new fashion in scientific thinking. The avowed object of his *Précis Élémentaire de Physiologie* (1816) was "to contribute to the introduction of the Baconian method of induction into physiological science".

Magendie was born in 1783 at Bordeaux, the son of a surgeon. He began his medical education under the informal system of the Revolution and completed it in the re-established Paris School under the tutelage of the

surgeon Boyer, being awarded the M.D. in 1808. Supporting himself by working as a prosector and lecturer in anatomy, he made his scientific débüt in 1809 by publishing a strong attack on the vitalistic concepts of Bichat, and in the same year read his first paper before the Paris Academy of Sciences in the presence of Laplace, Lamarck, and other great savants of the day. In his memoir on the chemical and physiological effects of strychnine he outlined clearly the methods which he was to employ in all his investigations and which became the cornerstone of experimental physiology. In 1813 he renounced surgery, resigned his position in the anatomical laboratory of the Faculty of Medicine, and started a course of private lectures in experimental physiology. He was exempted from military service through the intervention of the Academy of Sciences, and during the momentous events of 1815 he was able to work at the *Précis*, the first volume of which appeared in 1816. In 1821 he founded the first periodical devoted exclusively to physiology, the *Journal de Physiologie Expérimentale*, and in the same year he was elected to the Academy of Sciences and to the newly created Royal Academy of Medicine and Surgery. With the publication, in 1822, of his work on the function of the spinal nerve roots he reached the height of his powers, but owing to his liberal political ideas and somewhat uncompromising scientific attitude it was not until 1826 that he was appointed substitute physician at the Salpêtrière, and when the chair of medicine at the Collège de France fell vacant on the death of Laennec, Magendie was passed over although he had the almost unanimous backing of the Academy of Sciences. However, the revolution of 1830 brought an enforced vacancy of the chair and this time Magendie was appointed and at the same time was made physician at the Hôtel Dieu. From this point onwards he devoted himself to the practice of medicine, to the affairs of the Academy, and to the life of a country gentleman. He argued vigorously against the introduction of surgical anaesthesia, and the quarantine laws were considerably liberalized on his insistence that only typhus could be considered to be a contagious disease. He resigned from his hospital duties in 1845, and in 1852 he gave his last lecture at the Collège de France, being succeeded in the professorship by his assistant, Claude Bernard. He died in 1855 at the age of 72.

Magendie's greatest contribution to physiology, apart from the reintroduction of the scientific method, was his work on the direction of conduction in spinal nerve roots, in the demonstration of which his priority over Charles Bell is still disputed. Less spectacular, but of fundamental importance, were his researches in experimental pharmacology, while he made major contributions to our knowledge of the functions of the alimentary tract. Particular attention is paid in this paper to his contributions in the field of nutrition. In a memoir published in 1816 he distinguished between nitrogenous and non-nitrogenous foods and maintained that the tissue nitrogen was derived from food rather than from the air, describing animal experiments with nitrogen-free diets. Magendie drew special attention to the role of certain substances, particularly iodine, which furnish no energy but nevertheless contribute to the nutrition

of the animal. In 1841 he was a member of a committee of the Academy of Science which reported that gelatin, widely used at that time to replace meat, was virtually useless as a food, a fact which he had demonstrated 10 years previously. The up-to-date tone of his textbook is nowhere better illustrated than in the passage in which he discusses nutrients as being essential to replace substances lost in the ordinary wear-and-tear of metabolism.

W. J. Bishop

856. **Marcello Malpighi. II. Malpighi's Dealings and Correspondence with the Royal Society of London.** (Studi e ricerche su Marcello Malpighi. Nota II. Malpighi, i suoi rapporti e la sua corrispondenza con la Società Reale di Londra)

A. GALLASSI. *Rivista di Storia delle Scienze Mediche e Naturali* [Riv. Storia Sci. med. nat.] 41, Suppl. 1, 29-63, 1950. 40 refs.

The Royal Society was early to recognize the genius of Malpighi, and there were frequent interchanges of letters between him and the Secretaries of the Society which give a fairly full and chronological account of Malpighi's work and of the activities of other scientists. But although the Society published Malpighi's *Opera Omnia* in 1687, many of his letters were omitted, nor indeed have they been published in any subsequent writings on Malpighi. The University Library of Bologna contains a number of letters to Malpighi—some of them from Oldenburg, one of the Secretaries of the Society, and some signed by "J. Crawford", apparently a member of the English diplomatic service at Venice—together with autograph copies of his replies. That these have not previously been published may be because Oldenburg did not preserve copies of his own letters, while those of Malpighi never reached London.

After briefly describing the early history of the Society and the works which Malpighi submitted to that body, the author gives an account of the unpublished letters and the circumstances that prompted their writing. One of the letters from the Society contains an offer to publish Malpighi's work on the structure of plants and on the development of the egg. There are also two letters from Malpighi to Waller describing his work on the lymphatic system, in which he comments on the difficulties of corresponding abroad. The article concludes with the text of 17 previously unpublished letters.

H. P. Tait

857. **The Life and Time of Andreas Vesalius**

C. D. O'MALLEY. *Annals of Western Medicine and Surgery* [Ann. west. Med. Surg.] 5, 191-198, March, 1951. 5 figs.

858. **The Antiquity of Asaph the Physician and his Editorship of the Earliest Hebrew Book of Medicine**

S. MUNTNER. *Bulletin of the History of Medicine* [Bull. Hist. Med.] 25, 101-131, March-April, 1951. 17 refs.

859. **The Lifework of William Harvey and Modern Medical Progress**

H. P. BAYON. *Proceedings of the Royal Society of Medicine* [Proc. R. Soc. Med.] 44, 213-218, March, 1951.

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